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# THE VETERINARY RECORD

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## The Victoria Veterinary Benevolent Fund Christmas Appeal

AS the first letter to the Editor this week we publish an appeal from the President and two other Officers of the Victoria Veterinary Benevolent Fund. Its purpose is to ask the profession's support for the Fund's special Christmas activities, and we commend it warmly to everyone who reads these words. As will be seen it is suggested that veterinary surgeons should either make a monetary gift or one in kind, and among the shoals of appeals we shall all receive between now and the middle of December there can be none which will commend themselves more intimately to us all.

Loneliness and financial hardship are hard enough to bear at any time; but Christmas should see a determined effort by those whose lot is pleasant or whose means are sufficient to help their fellows: and it may be suggested that the direct personal gift offers the chance not merely of brightening someone else's Christmas in a material sense, but also of communicating a part of the spirit of the season by means of a letter or other message which may mean as much, perhaps far more, than the gift itself.

It must be remembered that the beneficiaries of the Fund, being the widows or children of veterinary surgeons, or members of the profession itself who have fallen on hard times through infirmity or age, are bound to experience the bitter comparison between the way of life to which they were accustomed as members or connexions of a not impecunious profession, and that which they now know. Never to have had the better things in life is bad enough: to have had them, and later lost them through no fault of one's own is worse.

Right resolutions, unless speedily carried into effect have a way of evaporating, and therefore we venture to urge our readers to do something in support of this Christmas appeal *now*.

But apart from this particular occasion, it is hoped that the profession will increase its general support of the Victoria Veterinary Benevolent Fund. Those who read the account of the Fund's activities published in these columns from time to time will have noted the lists of case reports which, necessarily brief as they are, illustrate the continuing and vital needs of those whom the Fund exists to help. It calls for little imagination to expand these laconic notes into terms of human hardship, illness and anxiety. Yet, because its means are limited, the help which the Fund can give is limited also. To anyone in dire need the gift of £50 or £100 a year may be a godsend—but such sums do not go far in these days, and it may be accepted that more would be done if finance allowed. It is unseemly that formerly active veterinary surgeons or their dependents should be, and should be seen to be, in poverty; and their more fortunate brethren are invited to come to their help in greater numbers.

One form of support which is of particular value is that by deed of covenant. In recent Minutes of one of the Fund's council meetings it was revealed that a mere handful of people covenant for annual subscription; yet by so doing they add very substantially to their donation at no extra cost to themselves. In addition, covenants enable the Fund's council to have a clearer idea of future income with all the advantages which that brings.

Nor should intending subscribers overlook the fact that for all veterinarians the Fund is, in a sense, a form of insurance; especially for younger men and women in these days of excessive taxation when saving on any scale is so difficult. Serious injury during practice, a motor accident, the flaring up of unsuspected illness can, in a moment almost, transform the prosperous and the successful into the anxious and the indigent.

There is no need to pursue the matter in further detail. The Victoria Veterinary Benevolent Fund has done, and continues to do a great work, bringing needed relief to many past members of the profession or their dependents, and reflecting great credit on the men and women who give so much time and thought, gratuitously, to raising funds, and distributing them wisely. The Fund's workers should be supported promptly and generously. Quite a small covenant from the majority of successful veterinary surgeons would transform the lives of many less fortunate, and the more who help the less will each individual donation need to be.

**Congress Paper read in Plenary Session**

# Recent Advances in the Control of Viral Epizootics by Vaccination Technique

BY

**H. S. FRENKEL**

**Blaricum, Holland**

THE subject is difficult, complicated and very wide ; and the difficulty starts in the first word of the title. What are we to understand by "recent" advances ? Where do "recent" advances begin ? When we consider that vaccination against smallpox was done by the Chinese some 2,000 years ago, we should call the vaccination technique of Jenner a recent advance. On the other hand time is moving so fast, and since the second World War science has made so much progress, that techniques of 10 to 15 years ago sometimes seem to be more or less obsolete.

However, when we look back on the last 200 years, we can assert that many successful vaccinations against viral diseases have been found without knowledge of viruses. The most important was achieved in this country. It was the great discovery by Jenner of vaccination against smallpox which protected the populations of the European countries from this dreadful disease. It has proved to be *the* weapon against smallpox, and still is the model of a live virus vaccine, even though we do not know exactly from which virus Jenner's attenuated strain originated.

Another vaccine of fundamental importance is that developed by Pasteur against rabies ; this was a live virus vaccine also, but attenuated artificially.

A virus disease banished from Europe is cattle plague. This, however, was not eradicated by vaccination, but mainly by sanitary and police measures. Some attempts, however, have been made to control it by vaccination and in this contest the work of a Dutch farmer named Geert Reinders is not generally known. He lived in the middle of the 18th century, and discovered a method of vaccination against cattle plague. He had observed that calves from cows that had recovered from this malady were immune from infection during the first half year of their lives. Reinders used this knowledge and immunised the calves actively by drawing through their skins a silver thread dipped in the nasal secretion of a diseased animal. This was one of the first combined immunisations, passive and active.

A second very important fact arising from Rynders' work is that of transferred immunity from mother to offspring, a phenomenon nowadays well established in many diseases and only recently observed in foot-and-mouth disease.

It is not my purpose to pass in review all viral diseases with their vaccination techniques ; but I think you will mainly be interested in those vaccination techniques with which I have been concerned personally. The Table below shows a number of animal virus diseases, with their vaccines, and these can be prepared either with live virus, attenuated virus or inactivated virus.

### Foot-and-Mouth Disease (F.M.D.)

Aphtisation has been carried out in some countries with the aim of shortening the illness in an infected herd. If there is no vaccine and no hyperimmune serum available, this method, though dangerous, has some advantages, provided that the hairless edge of the claws is kept disinfected, using tincture of iodine or another suitable antiseptic in order to prevent secondary infection.

A great number of vaccines have been developed against F.M.D. though not all of them are ripe for use in the field. The oldest vaccine is that of Vallée-Schmidt-Waldmann. Strangely enough Vallée never collaborated personally with Schmidt nor with Waldmann ; his experimental work on the inactivation of foot-and-mouth disease virus (F.M.D.V.) by means of formalin prepared the way for Waldmann, who ingeniously combined with Vallée's inactivation procedure Schmidt's important discovery—the adsorption of F.M.D.V. on aluminium hydroxide.

As a source of virus the living animal is used. It is extensively infected intradermo-lingually and the vesicles, fully developed 24 hours p.i., are harvested

TABLE I

| Foot-and-mouth disease | Hog cholera | Cattle plague | Vaccinia-cow pox |
|---|---|---|---|
| Aphtisation* | Rabbit† | Caprinised† | *Live virus* |
| Chick† | Crystal violet-field virus‡ | Lapinised† | Smallpox vaccine* |
| Unweaned mice† | Crystal violet-culture virus-sp'een tissue‡ | Chick embryo† | Vaccinia-cow pox vaccine* |
| Guinea-pig† | Spleen culture-virus adsorbed on alum. hydrox.‡ | Lapinised-av anised† | Chick embryo* |
| Rabbit† | | Lapinised-avianised-lapinised† | |
| Native virus (Val'ée-Schmidt-Waldmann)‡ | | | *Culture virus* |
| Bovine-, Ovine.-Swine fetuses‡ | | | Fetal bovine-fetal ovine skin* |
| Bovine tongue-epithelium‡ | | | Bovine tongue epithelium* |
| Bovine kidney‡ | | | |
| Swine kidney‡ | | | |

* = Live virus. † = Modified or attenuated virus. ‡ = Inactivated virus.

after slaughter and removal of the tongue. During the period between inoculation and death the animals are intensely diseased. A large number of cattle have to be infected to collect a sufficient quantity of virus for large-scale vaccination, and the whole procedure is not free from risk of spreading the disease unless strict measures can be taken to prevent escape of the virus. Countries using this method of virus production are obliged to consume the carcases to avoid excessive cost of vaccine production. The quality of the meat depreciates, and though it sterilises itself by the formation of lactic acid, a certain risk of spreading the virus remains, because of virus survival in bone-marrow and lymph glands.

In some countries where F.M.D. is endemic this method of virus production can be unsuccessful because of existing immunity, which prevents the virus partially, or even totally, from multiplication. Henderson (1960) remarks that attention must be paid to the possibility of type changing in bovine animals that have been exposed to infection ; this can happen when animals arrive at the slaughterhouse during the incubation period. In that case the blisters appearing after inoculation contain the virus of the natural infection.

The first cultivated F.M.D. virus capable of causing full development of the disease in cattle was produced in the State Veterinary Research Institute, Amsterdam (Frenkel & Waveren, 1935, 1937). It was started in tissue cultures of foetal bovine, ovine and porcine skin in the years 1933, 1934 and 1935. At that time we hoped that the serial cultivation of F.M.D.V. in a great number of transfers would modify the virus to an extent that it would lose its capacity to provoke the disease while keeping its antigenicity ; but culture virus produced in tissues of naturally susceptible hosts keep its pathogenicity.

For the production of F.M.D.V. on a large scale we could not rely on foetuses because of their scarcity. Meanwhile the antibiotics, a British discovery of tremendous importance, had been introduced in virus research. Antibiotics could not directly be used in the control of virus diseases, but they are of the highest importance in artificial cultivation techniques, permitting virus multiplication in tissues containing some bacteria. With the aid of penicillin, streptomycin and chloromycetin it became possible to grow the F.M.D.V. in bovine tongue epithelium. After disinfection of the tongue with 70 per cent. alcohol the superficial layer is discarded and the deep layers used for explantation and virus cu tivation. These layers are practically sterile. Formerly we believed that the epithelial tissue had to be minced, but further research proved that this is not necessary and that large sheets of tissue can be used equally well or even better.

At first the virus was grown in half-litre flasks but later in stainless steel containers of 60 to 600 litres, permitting the explantation of epithelial tissue from 50 and 500 adult bovine tongues (Frenkel, 1950; 1951).

This method of virus propagation, using sheets of tongue epithelium, is different from the procedure followed for example in the cultivation of polio virus. The latter is a real tissue culture followed by virus infection and can be considered as a multiple small-scale production, whereas the former is a direct mass cultivation.

The vaccine produced with the artificially grown F.M.D.V. is, except for some slight modifications, essentially the same as the Vallée-Schmidt-Waldmann vaccine. This culture-virus vaccine is exclusively used in our country. Practically the whole bovine population is vaccinated yearly in the period from February 15th to about May 1st. Animals below 4 months of age are not vaccinated. Born from immune mothers they have a passive resistance, *via* colostrum. Because of this temporary resistance we rarely see heart disease in these young animals, contrary to the pre-vaccination period when contact between a new-born animal and a diseased animal produces great danger of a deadly aphtous myocarditis. Incidentally our law prohibits movement of cattle that have not been vaccinated and this makes vaccination indirectly compulsory.

The results of this yearly immunisation are very satisfactory. Over a number of years only very sporadic cases of F.M.D. have occurred in our country. These cases are mostly observed in young non-vaccinated animals. Compared with several other European countries, the situation regarding F.M.D. is very favourable, especially considering the fact that Holland's geographical structure—no mountains, extensive meadows, dense human population, and large traffic—makes our livestock an easy prey for the F.M.D.V.

We have never seen any bad effects of mass-vaccination during the period of almost 10 years' application. The vaccination itself has never been the cause of death ; erroneous injection, on rare occasions, has caused fatalities.

It has been asked whether immunised cattle could not easily become carriers or excreters when infected with F.M.D.V. without showing any clinical sign. This can indeed happen with cattle that have recovered from the disease, or have been vaccinated.

" A rather large proportion of cattle, which have recovered from F.M.D., may still harbour the causative agent in the saliva during a period of several months. The virus may be demonstrated in material collected from the oesophagus by inoculation into unweaned mice or susceptible cattle. After contact with clinical cases, vaccinated animals may develop a similar carrier state without having shown symptoms of the disease. It is our experience that susceptible oxen kept in contact with such carriers remained unaffected, even if the oral cavity was swabbed with infective saliva. No cases of F.M.D. occurred in vaccinated or unvaccinated cattle or in unvaccinated pigs, if such animals were introduced into a herd known to contain carriers or if they were kept on the same premises with such animals.

" Our findings seem to warrant the conclusion that in cattle carrying F.M.D.V. a continual formation of small quantities of infective material is taking place. Purely mechanical carrying seems highly improbable " (van Bekkum *et al.*, 1959).

Every country has its own F.M.D. problem, depending, among other things, on its geographical

situation. Formerly, the policy followed in the Netherlands comprised the slaughter of all diseased and contaminated animals. As there was no natural protection, we were urged to stop this method of eradication which could even lead to the extermination of our whole bovine population. Mountainous countries are in a more favourable position : the valleys can be " locked up " to all kinds of traffic.

The United Kingdom has the good fortune to be surrounded by sea and also has the protection of mountains. Trouble seems to come mainly from the European continent, the infection being carried by birds, usually starlings, liking to spend their vacation in the milder climate of Great Britain. It seems, however, that this way of introduction of F.M.D.V. into Britain has diminished since vaccination has been applied on the continent.

Another regular source of infection coming from far distant would surely disappear if vaccination on a large scale were to be carried out.

The results obtained in Britain through the slaughter policy have been very satisfactory; and the costs of compensation have been rather low compared with the costs of systematic vaccination. However, if vaccination in this country were to be considered, systematic vaccination probably would not be necessary. If I may express my opinion, I would say that vaccination could be used in some special cases, for example when protection of non-contaminated precious herds was desired.

Many vaccines are available, between which a choice must be made. In addition to the two vaccines already mentioned other inactivated virus vaccines exist. They have appeared in very quick succession. Vaccines may be prepared from virus cultivated in bovine or swine-kidney cells but the difficulty with these vaccines is the necessity of tissue cultivation, which demands not only much work, but also is a slow method for obtaining the required quantity of virus. Using the method of cultivation in explanted surviving tongue epithelium, much troublesome work can be avoided. Instead of cultivating cells in glass containers and infecting them afterwards with virus, the bovine tongue provides us immediately with the cellular substrate.

Viruses that have been attenuated or modified by passage through non-naturally susceptible hosts also seem to be useful as vaccines. They are supposed to give a longer lasting immunity than vaccines composed with inactivated viruses, but it probably is premature to say that these vaccines are preferable to inactivated virus vaccines.

In our opinion the eradication of F.M.D., considered from a wide international standpoint, will best be achieved by the use of inactivated virus vaccines. The causal agent should not survive in any form on earth. Much research, however, will still be required to be sure that modified F.M.D.V. cannot recover its original virulence.

Some experience has already been acquired with virus passed through one-day-old chicks, unweaned mice, guinea-pigs, and rabbits. We know from the work of Vallée that guinea-pig-adapted virus does not immunise well, and from the work of Waldmann *et al.* that virus grown in foetal guinea-pig tissue is not of value either.

In our institute, Gillespie (1955) adapted a virus strain to the chick embryo and found that 2 bovine animals did not show clinical symptoms after intradermolingual infection with it, but were strongly immune.

Serial passages through mice, rabbits or chick embryos are attended with loss of cytopathogenic capacity in epithelial cells. It is difficult to say how many passages have to be accomplished to obtain the adequate modification. If serial passage has been continued too far, the capacity for immunisation may be lost.

Henderson (1960) reported that the 138th passage in rabbits immunised cattle poorly, whereas the 111th gave good results. Henderson states that though many strains have properly been modified, they cannot be used as vaccines until a number of questions have been answered satisfactorily. He may be right in saying that the new-born calf is susceptible to the pathogenic action of the modified virus in the same way as the unweaned mouse or rabbit. Therefore it is necessary to know at what age the calf loses this susceptibility and also if it is possible to vaccinate pregnant cows without endangering the calf. In many countries vaccination against the O, A, and C types of virus is necessary. Data do not exist about the possibility of inoculating with more than one living virus simultaneously, with resulting immunity for each separately. If several attenuated strains are simultaneously used, the possibility exists that only one causes a viremia and blocks the establishment of immunity against the other strains.

According to Henderson, the application of live virus vaccine in the field will depend on the possibility of its lyophilisation and whether more than one type can be used simultaneously. If the latter is not practicable, it would be necessary to vaccinate 3 times, if the presence of three types of virus is to be feared, with an interval of 2 to 3 weeks. In countries where vaccination of almost the whole bovine population is carried out, this triple vaccination would be impossible.

Though live virus vaccines against F.M.D. might give a longer lasting immunity than inactivated virus vaccines, we clearly can see that many difficulties for practical application are connected with them.

### Hog Cholera

Against hog cholera not so many vaccines exist, and only some of them are of value. The remaining vaccines have not yet passed the threshold of the laboratory. Among vaccines that have not yet finished successfully are two developed in our institute, *i.e.* a crystal violet inactivated culture virus vaccine, prepared with virus cultivated in explanted swine spleen tissue, and another on the same tissue basis inactivated with formalin and adsorbed on aluminium hydroxide (van Bekkum *et al.*, 1954).

The vaccines used in practice are : (1) Virulent virus plus antiserum ; (2) Crystal violet inactivated field virus vaccine ; (3) Lapinised live virus vaccine (with or without immune serum).

The live virus vaccines are produced by numerous passages of virulent virus through rabbits. The pathogenicity for swine is diminished and the antigenicity remains. They can be used with or without immune serum. Vaccines are also produced by alternating passages between rabbits and swine, using the last swine passage virus as a vaccine. It should be used with immune serum.

Lapinised live virus vaccine does not give complete protection immediately, when injected without serum, but seems to interfere rather soon with a natural infection. As soon as 2 days after inoculation, resistance has been observed.

The duration of immunity raised by modified virus vaccines is equal to those with combined virus immune serum treatment.

### Inactivated Virus Vaccines

Crystal violet vaccine is prepared from defibrinated blood of infected swine. Some vaccine producers add spleen pulpa, others lymphatic glands. This type of vaccine protects swine against artificial and contact infection. It is not active when used together with antiserum. Pregnant sows should only be vaccinated with live virus vaccine in the last 2 months. Vaccination of sows with live virus in the first month after mating gave ascites, subcutaneous oedema, and numerous abnormities in the foetuses including oedema of perirenal tissue and mesocolon, foci of inflammation in the liver, death and mummification.

Inactivated virus vaccines do not provoke these abnormities. They can be used without risk during the first month of gestation.

### Cattle Plague

During the second World War and after, a large number of vaccines were developed against cattle plague. All of them consist of attenuated (modified) viruses of different quality and must be carefully applied. They are not, at random, suitable for all kinds of bovine animals. They consist of virus that has been lapinised, avianised, lapinised-avianised, or lapinised-avianised-lapinised.

Other more frequently used vaccines are prepared from inactivated virus-containing tissues. These vaccines immunise, but have some disadvantages compared with the recently developed modified virus vaccines in that they are expensive, yielding only 100 to 300 doses per donor animal, and keeping their potency only 4 months when stored. Usually 2 to 3 doses of 1 0 ml. injected with an interval of one week are required to establish immunity, which lasts 8 to 10 months against field exposure and a much shorter time when challenged by injection of 1,000 to 10,000 M.L.D. of virulent bovine virus. A recently developed heat inactivated tissue vaccine combined with adjuvants (mineral oil and mycobacterium) has more significance. From a bovine spleen weighing 500 g., 1,500 doses can be produced. It is inactivated by 1 per cent. formalin and can be stored under refrigeration for 8 months. When administered subcutaneously it raises a strong purulent reaction.

The modified virus vaccine produced by serial passage through goats is too virulent for European cattle. In the more resistant indigenous animals it gives a 3- to 5-year immunity.

Kabete-attenuated goat virus has been shown to be able to check the spread of infection within affected herds by interference, several days before a protecting quantity of antibody has developed. It is prepared from goat spleen on the 3rd day of temperature rise.

Numerous passages through rabbits (700 to 800) give the virus a fixed virulence for this species and a fixed attenuation for bovine animals. This attenuation goes farther than that of the Kabete vaccine and therefore is more suitable for use in European cattle, though it seems too weak for indigenous animals. (Spleen, mesenteric glands and blood are collected 3 days after infection, and minced in a Waring blender together with saline to a concentration of 20 per cent. To the pooled virus of 10 rabbits 200,000 units of penicillin are added. One rabbit yields 500 to 1,000 doses. Lyophilised and sealed in ampoules it keeps its viability when stored at –25° C. for 2 years. Immunity, because of interference, develops within 4 to 5 days. Nakamura and Miyamoto (1960) have obtained a further attenuation by serial passage through embryonated chicken eggs (lapinised-avianised vaccine).

During the second World War a combined American-Canadian group of virologists under the direction of Shope, successfully adapted cattle plague virus to embryonated eggs. This vaccine has not been extensively used because the original strain was lost.

To my knowledge no attempts have yet been made to produce the virus in tissue cultures or in surviving tissue, *e.g.* in epithelial cells of adult bovine tongues as is done for the cultivation of F.M.D.V. In my opinion it would be worth while to try this type of virus growing. It would not necessarily demand epithelium, but could also be carried out with mesenchymatous tissue, or with a mixture of both, because cattle plague virus is not specially epitheliotropic.

### Vaccinia and Cow-Pox

As already mentioned small-pox in man is controlled with vaccinia virus. Usually this virus is produced following cutaneous inoculation of calves, buffaloes, or sheep. For many years the same procedure has been used.

Though the benefit of Jenner's classic discovery is immeasurable, and vaccination according to this more or less unchanged method still is of the highest value to mankind, the study of this vaccination is continued. The discovery of the chicken egg as a biologic individual offering great possibilities in virus research as well as in large-scale virus production, has stimulated the imagination of many virologists. Equally, or even more important, has been the introduction of cell and tissue explantation.

Based on the fact that multiplication of viruses happens exclusively in living cells, many investigations have been carried out in growing viruses outside the living animal in cells or tissues kept alive *in vitro*. Besides the classic vaccines, mentioned above, a chick embryo vaccine has been created; three

other vaccines have been developed in our Institute, one with explanted foetal bovine skin, a similar one in the foetal ovine skin, and finally one in explanted bovine tongue epithelium. Of these three vaccines, the one produced with virus grown in sheets of bovine tongue epithelium is the most promising, because of the availability of bovine tongues (Frenkel *et al.*, 1936 ; Frenkel, 1957).

Vaccine prepared from culture virus has many advantages over the classic vaccine in that it is bacteriologically sterile and immediately ready for use after having passed the necessary tests for potency and bacteriological sterility. For the production of this vaccine no expensive installations are required. It is prepared mixed with glycerine as usual, or lyophilised without the addition of glycerine. Subcutaneous or intradermal inoculation can be considered. It has an average titre of 5 to 9 times $10^7$ infective units per ml.

The future will tell us if this type of vaccine, which is prepared from the same host-tissue as the Jenner vaccine, will be used in practice.

In veterinary practice the vaccine can well be used in outbreaks of vaccinia or cow-pox infections. In a few sheds where a number of cows showed vaccinia, the uninfected cows were successfully immunised by subcutaneous injection.

The effects of inactivated culture vaccinia virus have been tested in humans after intracutaneous injection. Following two or three injections the volunteers had neutralising antibodies in their blood serum. If a better inactivation procedure is found, permitting a sufficient antibody formation after one injection, it could be used as an introductory vaccination, followed by a virulent cutaneous inoculation. Would there be less chance for the development of post vaccinal encephalitis ?

Before finishing this incomplete account I would like to say a word on future possibilities. Biochemical research on viruses and cells and their interrelationship is growing very fast, side by side with biological studies. The knowledge of what happens in the virus-infected cell is increasing, though much of it still belongs to the field of speculation. Some facts seem to point towards a possible influencing of the cell metabolism in the way that intracellular production of virus is prohibited.

I have no idea how far in time we are separated from this point, but until then we continue to rely upon the formation of antibodies generated by our vaccines.

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## LIVESTOCK NUMBERS INCREASE

September returns for farming in England and Wales—estimates from a one-third sample of holdings—show increases in all classes of stock:—

Cows and calves totalled 8,789,000 against 8,734,000 in September, 1960, and 8,565,000 the year before that. The breeding herd of beef-type and dairy-type cows is up by 134,000 (4.2 per cent.). Dairy cows and heifers in-milk were up over the year from 2,082,000 to 2,163,000. Those mainly for raising beef calves increased from 442,000 to 458,000. Calves less than a year decreased by 80,000 to 1,913,000.

The year's increase in sheep was from 15,874,000 to 16,501,000. Within the total, breeding ewes advanced by 4.4 per cent. from 6,915,000 to 7,217,000. Lambs on farms increased by 6.5 per cent. to 6,648,000.

The returns revealed a 10 per cent. increase in sows for breeding—from 577,000 to 638,000—and 25,000 of the increase were recorded since June. Total pig population reached 5,166,000 against 4,666,000 in September, 1960, and 4,920,000 in September, 1959.

The numbers of poultry over 6 months old increased from 42,592,000 to 43,770,000 and those under six months from 33,762,000 to 40,052,000. Among the latter, young birds for breeding or egg production increased from 14.34 million to 16.93 million and those for broilers from 15.06 million to 18.56 million. The year's increase in turkeys was 37 per cent.—from 4.01 million to 5.51 million.

# The Diseases of Broiler Rabbits

BY

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*SUMMARY.—The results of a survey of losses in a rabbit broiler unit are presented, and the major problems discussed in relation to the literature. Other conditions seen, or thought likely to arise are briefly described. Details of normal rabbit husbandry under different systems of broiler-production are outlined.*

## General Introduction

THE European rabbit (*Oryctalagus cuniculus*), has been domesticated for hundreds of years. Prior to myxomatosis occurring in Britain there was a steady demand for fresh and frozen imported carcases but the widespread incidence of the disease caused a general repugnance to the meat of the wild rabbit. There is now a good market for the broiler rabbit. A well-established meat rabbit industry exists in the U.S.A., Scandinavia and the Low Countries. Foundation breeding stock has been imported from these countries during the last 3 or 4 years to establish the industry in Britain. As with any intensive method of animal production, the prevention of disease, early accurate diagnosis and prompt control measures based on knowledge of the species and commercial practice are important in maintaining the production of an economic wholesome product. The veterinary clinician and laboratory worker have each an important rôle to play in assisting an industry which is still very much in its teething stage. This paper is intended as an introduction to the methods used for the intensive production of the young meat or broiler rabbit. It has been written with the aim of providing an outline of the husbandry methods for the veterinary practitioner who is approached for advice for the first time. An attempt has been made to select those diseases which could be of particular importance to the industry. For further information the writer would refer readers to useful books by Blount (1957) and Sandford (1957) and the section devoted to the rabbit in the book by Worden and Lane-Petter (1957) all of which have been freely consulted during the preparation of this paper.

## The Normal Rabbit

At the present stage, the New Zealand White, the Californian and the Dutch rabbit are the principle breeds used to produce the broiler rabbit. Breeders, with the help of geneticists, are hoping ultimately to produce a standard hybrid rabbit. The rabbit should be 3 to 5 lb. live-weight in the New Zealand White rabbit and less in the smaller breeds. They may be sold directly from the doe on weaning at 8 weeks, or on reaching the correct weight if weaned early. The emphasis is on carcase quality and the pelt has a relatively low value.

*Husbandry*

As broiler rabbit production is a new industry in this country, it was thought that it would be helpful to outline the systems of husbandry, and some other points of interest so that the problems could be more clearly appreciated.

The work and capital involved are important considerations in deciding the most suitable animal accommodation. The rabbit may be kept on wire floors or solid floors. Tiered battery cages similar in principle to hen-laying batteries (Fig. 1) or less elaborate cheaper wooden framed structures may be used. The cages have galvanised welded wire mesh floors, the mesh commonly measuring 1 inch by $\frac{1}{2}$ inch or $\frac{3}{4}$ inch by $\frac{3}{4}$ inch. The ideal gauge of wire is still undecided, but 14 to 16 is usual. Individual compartments are usually made large enough for a doe and her litter to 8 weeks old. Water may be supplied by continuous droplet, although some breeders question whether a heavily lactating doe can maintain an adequate water intake by this method of supply and use individual containers for each cage. Paterson (1956) dislikes open crocks and suggests glass drinking bottles with metal drinking tubes set in rubber corks. He uses a metal pellet hopper with a sieve bottom to prevent the food caking and a hole large enough for the head situated 9 to 10 inches above floor level, which prevents faecal contamination and early feeding by the litter. It is important to check regularly that pellets are being supplied by the hopper, as an obstruction to the downflow can occur. A rack is provided if hay is fed. Droppings and urine fall through the floor on to a scraper board running the length of the battery. The nest box is usually removable and of varying design. It may be enclosed with an open end or a simple open-topped box. Disposable boxes are proposed, or part of the compartment may be sectioned off and concealed by a hanging sheet. Hutches can be made from wire mesh on a timber frame, the hutches being placed in racks with trays to catch the dung and urine. Producers may use solid floor hutches or colony pens on the ground.

Opinion differs in the industry as to the relative merits of wire-mesh floors, solid floors and colony pens.

Wire-mesh floored hutches allow the faeces and urine to escape immediately as long as hay or bedding or corners do not form a collecting point, though the young rabbit will obviously not benefit from the system until leaving the solid-floored nest. Coccidiosis is not eliminated but the level of infection is considerably reduced and a coccidiostat, fed con-

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tinuously, is probably not essential if the standard of hygiene is high. General activity is apparently less on a wire floor and this may possibly be reflected in the health of the adult. Sore hocks are more common. It is suggested that so-called "mucoid enteritis" may also be a greater hazard. Conception is said to be lower in winter than on solid floors as the does are less receptive.

Solid-floor hutches are more comfortable, there is more general movement and sore hocks are not generally a problem. Greater attention to hygiene is required with fairly frequent additions of bedding. The continuous administration of a coccidiostat is probably essential. The winter conception rate is higher than on wire floors. Labour requirements are greater.

Rabbits may be reared on wire floors and transferred to solid floors for breeding.

Colony ground pens allow several early weaned litters to be reared together in a group, fresh bedding being added as necessary. Group mating reduces the labour involved.

*Environment*

This may vary between dependence on natural ventilation through open eaves, and the provision of a controlled environment with artificial heat and powered ventilation. The wild rabbit is biologically successful throughout the world under temperate and sub-tropical conditions. It objects to wet and cold. The writer is not aware of any figures which have been produced to indicate the optimal ventilation rate or humidity level. Paterson (1956) states that rabbits do not relish extremes and the benefit of well-ventilated houses is emphasised. It is suggested that 50 deg. F. is the optimum temperature with as little fluctuation as possible. It is probable that poor ventilation, possibly with detectable ammonia in the atmosphere, can result in a high incidence of respiratory disease and present a serious hazard to economic rabbit production.

Sudden disturbances in the rabbitry should be kept to a minimum. The domestic rabbit is stimulated by noise, to stamp its hind legs in fright, and this can result in damage to the individual, and trampling or scattering of the young.

*Alimentary Tract*

The rabbit has rodent teeth and food is well masticated. It is an almost continuous feeder and up to 80 feeds of varying sizes may be consumed in 24 hours. Blount (1957) considers that catarrhal material is normally present on the gastric mucous membrane one hour after death and that an empty stomach or fluid contents are abnormal. Leontyuk (1959) found that the stomach took approximately 72 hours to empty. It has been shown radiologically by Klarenbeek (1947) that acute pyloric spasm is not uncommon. The rabbit does not vomit. Heavy bile production is a digestive feature. The large intestines are voluminous with a mesenteric lymph gland which may be involved in several diseases. The quantity of faeces produced by a healthy rabbit varies considerably with the total food intake, particularly with the amount of fibre.

*Faecal Pellets*

Two forms of pellets are normally produced. Soft small pellets are produced at night and normally re-ingested, the rabbit collecting them from the anus. These pellets may be interspersed between the usual harder ones. This habit results in improved digestion and a considerably increased supply of the vitamin B complex. It is suggested by Blount (1957) that as the rabbit's stomach has little power of contraction, coprophagia is a means of providing bulk upon which the stomach muscles can act.

*Diet*

A carefully balanced ration based on a knowledge of the requirements of the species is essential if the rabbit is to be maintained in good health while being subjected to the methods of intensive production. As yet there is relatively little information on rabbit nutrition as compared with poultry. A non-pregnant doe or one in the first half of pregnancy may be rationed to 4 or 6 ounces of pellets a day. The pregnant doe's requirements for energy and protein increase during the second half of pregnancy to twice maintenance at parturition. A suckling doe is fed *ad lib.* and requires three times maintenance during the first weeks of lactation, increasing to four times and higher after 3 weeks. The protein requirements in the early stages of growth of the young rabbit are higher than those for maintenance of the adult. Worden and Lane-Petter (1957) deal with the calculation of calories and protein requirements in some detail. Templeton and Kellogg (1959) specify one ration containing 12 per cent. to 15 per cent. protein and 20 per cent. to 27 per cent. fibre for dry does, herd bucks and developing young, and a second containing 15 per cent. to 20 per cent. protein and 14 per cent. to 20 per cent. fibre for pregnant and milking does. By this means it is easier to prevent does getting over-fat.

When one pellet formula is available, *ad lib.* feeding may lead to does becoming excessively fat and breeders frequently restrict the ration of does in the early stages of pregnancy. Excessive weight appears to be more of a problem when the litter is weaned at 8 weeks than when early weaning and remating is practised at 3½ weeks. Working bucks are more commonly fed *ad lib.*

At the moment several British manufacturers produce one pelleted complete food but as demand increases more work will have to be carried out on the nutritional requirements of the rabbit.

If hay is fed it should be leafy, green and free of mould. The water supply must be continuous. A 10 to 12 lb. doe and her litter of 7 at 7 to 8 weeks of age can drink a gallon of water in 24 hours.

*Breeding*

*Does.* These are normally ready for service at 4 to 6 months with some latitude according to the breed. Domestic rabbits kept under optimum conditions of temperature and nutrition will breed throughout the

year with a seasonal winter depression. A conception rate of 75 per cent. to 90 per cent. is common. Oestrus was thought by Brambell (1948) to be more or less continuous, with a set of mature follicles always ready to ovulate and a fresh set developing every 7 days. It is suggested by Templeton and Kellogg (1959) that there is a 15 to 16 day cycle, and conception can occur during the middle 11 or 12 days. As a general rule the vulval mucous membrane is pale and dry when the doe is not receptive and congested and moist when she will permit coitus. Copulation, or a strong sexual stimulus is necessary to cause ovulation, this occurring 10 hours later.

*Bucks.* These mature about the same age as the does. One buck is normally kept for every 10 to 15 does. Services are generally restricted initially, after which a buck appears to be able to maintain a satisfactory conception rate when serving up to two does a day. The doe is taken to the buck as the reverse leads to fighting. If the doe is not fully receptive, there may be some sex play possibly including epiuresis, when the buck sprays urine on to the doe and around the cage. Service is rapid and may be repeated in less than a minute. On completion, the buck commonly falls on his side with a squeal. In some instances the doe may be restrained for service.

Another system is to put a buck with 4 does for 4 days, during which time does are served several times and a conception rate of 90 per cent. is possible. Bucks may be worked on alternate fortnights in this system. Oestrus terminates following ovulation, but the doe will frequently permit copulation during pregnancy and pseudo-pregnancy. The gestation period for domestic rabbits is 30 to 32 days. Pseudo-pregnancy lasts 16 days and follows ovulation without implantation. At the end of the pregnancy or pseudo-pregnancy the doe plucks fur, makes a nest and has colostrum. To avoid sex play between does and possible ovulation, does that are to be mated are put into individual cages 3 to 4 weeks before service so that they have passed through any pseudo-pregnancy after which they are particularly fertile.

*Pregnancy Diagnosis*

Test-mating, *i.e.*, placing the doe with the buck at 16 to 17 days after service to observe whether or not the doe is receptive is not a satisfactory criterion, though it is commonly practised. Some pregnant does will permit service and others will not when they have not conceived. Pregnancy can be diagnosed by palpitation of the abdomen from the seventh or eighth day, with 14 days as the optimum time (Suitor, 1946). One large breeder thought that the number of abortions increased following routine pregnancy diagnosis. Foetal re-absorption is of high incidence in the wild rabbit but does not appear to be important in domestic rabbit production. Antibody passage is thought to occur mainly, if not entirely, before birth.

*Parturition*

On wire floors a nest box of sufficient size is given 5 to 7 days before parturition, with litter for nest building. The fur normally loosens on parts of the body around parturition time, and is plucked to line the nest. Sawin and Crary (1954) consider there is a relationship between the quality of nest building and mothering ability.

Rabbits are born hairless, blind and deaf, and the eyes open on the tenth or eleventh day. The placenta and foetal membranes are eaten by the doe and the umbilical cord severed. Occasionally and more commonly in young does this extends to cannibalism, and in addition the litter may be scattered. Litter scattering is considered by some breeders to be more prevalent on wire floors. On a solid floor a doe may divide a large litter between 2 nests. The doe has an average of 8 teats which the young freely exchange. Adams (1961) has observed that if only one or two foetuses develop parturition may not result and mummification causes sterility.

Though traditionally early examination of the young is said to encourage cannibalism, one New Zealand White rabbitry practised weekly litter weighing from day-old without causing this vice. The nest should always be quietly examined for decomposing dead. Litters obtained by caesarean section have been hand-reared satisfactorily (Hills and McDonald, 1956). Rabbit milk contains 10 per cent. protein as compared with 4 per cent. in cow's milk. To increase the percentage of protein, calcium caseinate was added to cow's milk at the rate of 15 gr. to 10 ounces of cow's milk. After 7 days it was necessary to increase the amount to 17 gr. for every 10 ounces and after 14 days this was again increased to 20 gr. The last level was maintained until the rabbits were weaned at 4 weeks. At 3 weeks of age the hand-reared rabbits were approximately 300 gr. as against 500 gr. for those reared naturally. The calcium caseinate did not dissolve freely and had to be whisked in. The mixture kept for several days in a refrigerator and was warmed by immersion in hot water. Feeding bottles with teats, as used for dolls, were obtained and some knack was required to insert the teat between the upper jaw and tongue. The rabbits were given as much as they would take at 3-hourly intervals with a final feed at midnight and the first between 5 and 6 a.m. They were kept in a box lined with hay and cotton wool.

A common litter size is 8 to 10 for the New Zealand White, and 6 for the Californian. Breeders aim at weaning 25 to 30 young per doe per annum from 4 or 5 litters. Newly-born rabbits can be transferred to other does, during the first few days, if the mother dies, or the litter is large, by mixing the litters together in a nest box and keeping the doe away for a time. The young should not vary more than 3 or 4 days in age. A litter remains in the nest box for approximately 3 weeks, an earlier exit suggesting a shortage of milk. Weaning may be gradual, the litter remaining with the doe to 8 weeks of age, when those not required for rearing are slaughtered. The doe will have been re-mated at approximately 6 weeks *post partum*. Some breeders consider it is economically essential to mate virgin does at 16 weeks old, weaning and re-mating at 3 to 4 weeks after parturition, the weaned rabbits being reared to meat

weight in groups of 30 to 40. At least one large breeder appears to have practised this system satisfactorily. The industry has not been established long enough for all the aspects of a breeding system to have been critically analysed, particularly with regard to the numbers reared and the productive life of the does. It will be noted that an opportunity for transference of disease by contact occurs during (i) mating, coitus and sex play, (ii) the fostering of young, (iii) mixing of litters for rearing purposes.

*Examination of Stock*

The ideal way to hold an adult rabbit is to grasp the fold of skin over the shoulders and use the other hand to support the rabbit under the rump. Handling any other way may lead to injury. The writer has had a valuable buck suddenly move with a resultant fractured vertebra. A visual examination can reveal poor body condition, any abnormal discharges, spirochaetosis (venereal disease), ear-canker, sore hocks, snuffles, overgrown teeth, mange, ringworm, abscesses and mastitis.

Tattooing of the ears or ear tagging are the usual methods of identification.

*Ageing.* The first pre-molars are replaced by permanent ones at 25 to 26 days. The epiphyseal gaps close at the forty-fourth week. Prior to this the gap can be felt by running a fingernail down the front of the tibia. Full-grown rabbits cannot be aged.

*Sex.* The sexes can be differentiated from day old but it is easier at 8 weeks. The external genitalia are very similar in the immature rabbit. Gentle pressure exposes the mucous membrane which in the buck forms a circle and in the doe a slit.

*Clinical Data.*

Rectal Temperature: 102.5° to 103° F.
Femoral Pulse Rate: 80 to 120 per minute.
Respiratory Rate: 36 to 56 per minute.

*Suggestions for the Prevention of Disease*

(i) The purchase of vigorous stock.
(ii) The early culling of ailing stock. Hospitalisation is to be deplored as it increases the risk of disseminating disease from a focal point. Dead or ailing animals should, of course be handled last.
(iii) Quarantine of all new stock for at least 2 weeks.
(iv) Well designed, adequately ventilated and easily disinfected houses. Several small houses seem preferable to one large unit as far as disease control is concerned.
(v) A high standard of management and hygiene with stockhandling kept to a minimum.
(vi) Wholesome food of constant composition. As a guide, preferably not more than a month's supply of pellets should be purchased and stored in cool, dry surroundings to maintain quality.
(vii) Vaccination with a myxomatosis vaccine if this is considered a justifiable expense.

*Disinfection.* A 10 per cent. solution of commercial or household ammonia should be used to destroy coccidial oocysts. Otherwise there are no particular recommendations for disinfection and standard practices can be followed. Formaldehyde applied as an aerosol by means of a Microsol "2 oz." generator is an effective method for disinfecting large buildings (Harry, 1961).

*Anaesthesia*

Induction by intravenous pentobarbitone sodium given slowly into an ear vein and transferring to ether by inhalation has given consistently good results for abdominal operations lasting 30 minutes or so (Adams, 1961). The corneal and pedal reflexes are used as a guide to the depth of anaesthesia, particular attention being necessary during induction and changing to ether, when respiratory failure is a hazard. This method has led to viable young following caesarean section. Induction by ether alone produced a period of excitement but can be used for very young rabbits.

*Artificial insemination*

This has been practised successfully. A teaser doe is used and a buck will ejaculate into an artificial vagina sufficient semen to inseminate approximately 20 does, when diluted up to 15 times. Ovulation can be stimulated by an hormone injection or by mating with a vasectomised buck and sometimes by mechanical stimulation as in the cat. The doe is then inseminated in the usual manner. One advantage of using artificial insemination is that a breeder with only a small number of bucks could arrange for a large number of does to kindle within a short period, thereby ensuring a large and attractive consignment of meat rabbits for collection by the packing station.

## RABBIT DISEASES

### Introduction

Approximately 18 months ago the writer had the opportunity of examining casualties from a large modern rabbitry using the battery system with wire floors. In view of the expanding industry and the likelihood of a growing demand for advice it was decided to examine a series of rabbits *post-mortem* for comparison with the figures of an American worker, Lund (1951) who reported on the total casualties of a rabbitry over a 3-year period. Approximately 600 rabbits of all ages have been examined, most of which had been dead for at least 24 hours. The time available for *post-mortem* and ancillary examinations was dictated by the varying amount of general diagnostic material arriving at a veterinary investigation centre. Fewer carcases were examined during seasonally busy periods and this may influence the recorded incidence of some diseases. The routine adopted was an initial gross *post-mortem* examination; films of the intestinal mucosa were examined for coccidial oocysts; the heart blood, liver and intestinal contents were cultured onto 5 per cent. sheep blood agar and desoxycholate citrate agar, and incubated aerobically at 37°C. for 16 to 18 hours; other examinations were carried out as indicated by the general *post-mortem* examinations.

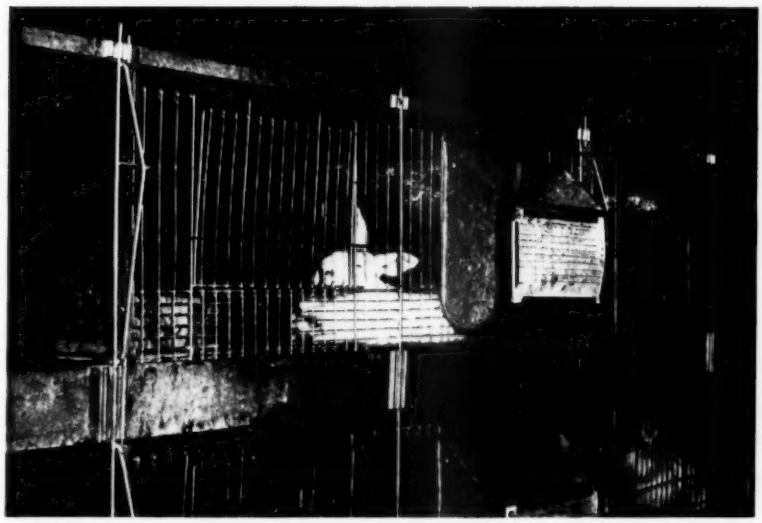

Fig. 1. Typical wire-floor cage unit showing nest-box and food and water containers.

Fig. 3. Rabbit kidneys showing advanced lesions of nephritis.

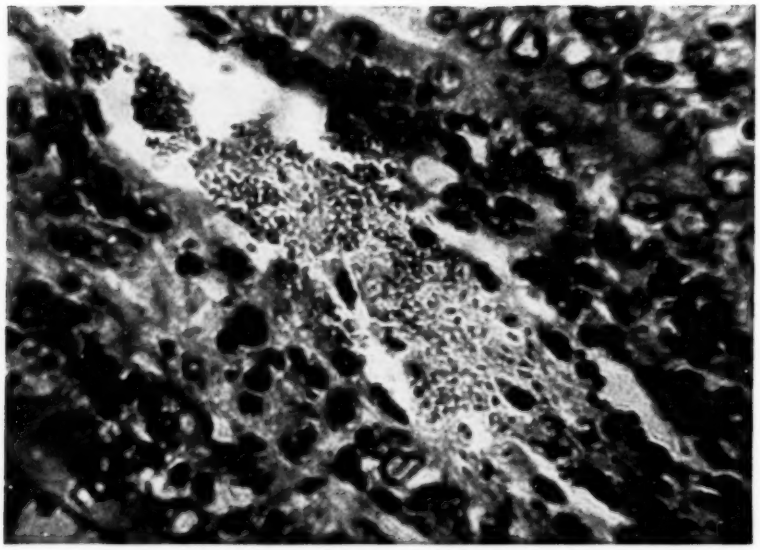

Fig. 4. Section of rabbit kidney showing organisms like *T. gondii* in lumen of tubule. X 400 Stained Weil-Weigert.

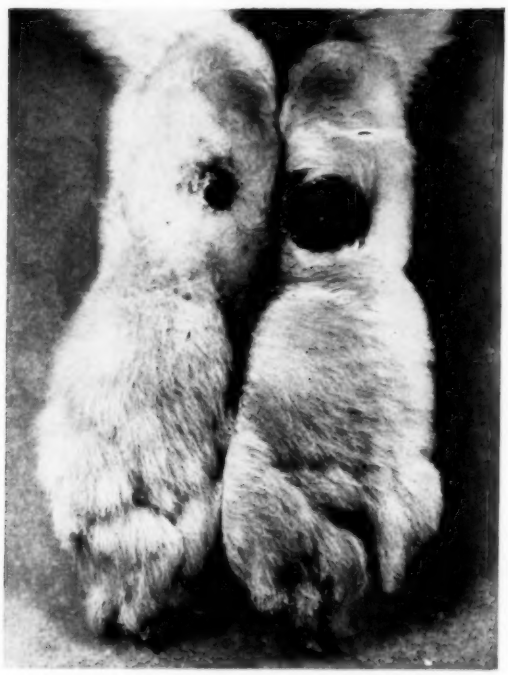

Fig. 5. Ulceration of the plantar surface of the metatarsal area, typical or sore hocks.

## RESULTS

The *post-mortem* findings are presented in table form. Table I shows the incidence of each disease from birth to over 2 years expressed as a percentage of the total number rabbits affected. Table II shows the distribution of the diseases in each age group expressed as a percentage of the number of cases in the group.

It will be seen that more than one system was frequently affected so that it was often difficult to decide which were the primary lesions.

*Groups 0 to 3 weeks (30 Animals)*

This period is normally spent in the nest box. Relatively few rabbits were examined in this group but it is generally considered that mortality does not

TABLE

INCIDENCE OF DISEASE FROM BIRTH TO OVER TWO YEARS EXPRESSED AS A PERCENTAGE OF THE TOTAL NUMBER OF RABBITS AFFECTED

| | 0—3 weeks | 4—8 weeks | 9 weeks to 6 months | Over 6 months to 1 year | Over 1 year to 2 years | Over 2 years | Total | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. | Per cent. |
| Enteritis | 3·3 | 48·3 | 45 | 0 | 3·3 | 1·1 | 89 | 15 |
| Caecal Impaction | 8·3 | 25 | 66·7 | 0 | 0 | 0 | 12 | 2 |
| Gastric Haemorrhages | 7·2 | 21·4 | 50 | 14·2 | 7·2 | 0 | 14 | 2·3 |
| Typhlitis | 4·5 | 67·5 | 28 | 0 | 0 | 0 | 22 | 3·6 |
| Pneumonia and Enteritis | 0 | 82·3 | 11·8 | 0 | 0 | 5·9 | 17 | 3 |
| Pneumonia (including Empyema) | 0 | 26·5 | 60 | 11·5 | 2 | 0 | 98 | 17 |
| Pneumonia + Caecal Impaction | 0 | 16·7 | 77·8 | 0 | 0 | 5·5 | 18 | 3· |
| Pneumonia + Nephritis | 0 | 0 | 43 | 57 | 0 | 0 | 7 | 1·1 |
| Pneumonia + Other* | 0 | 22·2 | 44·4 | 22·2 | 0 | 11·2 | 17 | 3 |
| Nephritis | 7·2 | 2·8 | 23 | 28·5 | 28·5 | 10 | 70 | 11·2 |
| Nephritis and Fur Ball | 0 | 5 | 0 | 70 | 25 | 0 | 21 | 3·5 |
| Fur Ball | 20 | 0 | 6·7 | 53·3 | 20 | 0 | 15 | 2·5 |
| No Diagnosis | 14·4 | 20·1 | 29 | 26 | 7 | 3·5 | 104 | 17·3 |
| Arthritis | 0 | 0 | 11·1 | 55·6 | 33·3 | 0 | 9 | 1·5 |
| Arthritis + Staph. Nephritis | 0 | 0 | 5·5 | 39 | 39 | 16·5 | 18 | 3 |
| Gastric Haemorrhages + Nephritis | 11·1 | 11·1 | 22·2 | 22·2 | 33·4 | 0 | 9 | 1·5 |
| Metritis | 0 | 25 | 25 | 25 | 0 | 25 | 4 | 0·6 |
| Mastitis | 0 | 20 | 0 | 20 | 60 | 0 | 5 | 0·8 |
| Miscellaneous | 0 | 29·2 | 25 | 16·6 | 25 | 4·2 | 24 | 4 |
| Nephritis + Others* | 0 | 26 | 10 | 40 | 24 | 0 | 19 | 3 |
| | | | | | | | 596 + 4 = 600 | |

TABLE II

DISTRIBUTION OF DISEASE IN EACH AGE GROUP EXPRESSED AS A PERCENTAGE OF THE NUMBER OF CASES IN THE GROUP

| Disease | 0—3 weeks | 4—8 weeks | 9 weeks to 6 months | Over 6 months to 1 year | Over 1 year to 2 years | Over 2 years | |
|---|---|---|---|---|---|---|---|
| Enteritis | 10 | 28·6 | 18·6 | 0 | 4·5 | 6 | |
| Caecal Impaction | 3·3 | 2 | 3·6 | 0 | 0 | 0 | |
| Gastric Haemorrhages | 3·3 | 2 | 3·1 | 1·8 | 1·5 | 0 | |
| Typhilitis | 3·3 | 10 | 2·7 | 0 | 0 | 0 | |
| Pneumonia and Enteritis | 0 | 9·3 | 0·8 | 0 | 0 | 6 | |
| Pneumonia (including Empyaemia) | 0 | 17·3 | 27 | 9·4 | 3 | 0 | |
| Pneumonia + Caecal Impaction | 0 | 2 | 6·4 | 0 | 0 | 6 | |
| Pneumonia + Nephritis | 0 | 0 | 1·3 | 3·5 | 0 | 0 | |
| Pneumonia + other* | 0 | 2·5 | 3·5 | 3·5 | 0 | 0 | |
| Nephritis | 16·8 | 1·3 | 7·3 | 16·9 | 30 | 35 | |
| Nephritis and Fur Ball | 0 | 0·6 | 0 | 11·6 | 9 | 0 | |
| Fur Ball | 10 | 0 | 6·3 | 6·7 | 4·5 | 0 | |
| No Diagnosis | 50 | 14 | 14·4 | 22 | 10 | 20 | |
| Arthritis | 0 | 0 | 0·3 | 4·3 | 4·5 | 0 | |
| Arthritis + Staph. Nephritis | 0 | 0 | 0·3 | 5·7 | 10 | 15 | |
| Gastric Haem. + Neph. | 3·3 | 0·6 | 0·8 | 1·8 | 4 | 0 | |
| Metritis | 0 | 0·6 | 0·3 | 1·0 | 0 | 6 | |
| Mastitis | 0 | 0·6 | 0 | 1·0 | 4 | 0 | |
| Miscellaneous | 0 | 4·6 | 2·7 | 3·5 | 9 | 6 | |
| Nephritis + others | 0 | 3·3 | 0·8 | 6·9 | 6 | 0 | |
| | 30 | 150 | 207 | 117 | 65 | 20 | 596 + 4 = 600 |

usually exceed 5 per cent. of live births during the period.

The fact that no diagnosis was made in 50 per cent. (15 cases) of those examined suggests that poor mothering, litter scattering, chilling, or lack of milk may have been partly responsible for death. Enteritis was present in 23 per cent. (7 cases).

*Group 4 to 8 weeks (150 Animals)*

The number examined in this group represented 25 per cent. of the total. This is the 4-week period during which the rabbits have left the nest to be fully subjected to the environment of the rabbitry and at the same time are eating an increasing amount of solid food. It is also the period when coccidiosis or other disease contracted during suckling might be a significant cause of disease. These facts appear to be related to the incidence of enteritis and pneumonia, as they were common from the fourth week with enteritis predominating to the seventh week (see Fig. 2).

*Group 9 weeks to 6 months (207 cases)*

The number examined in this group represented approximately 34 per cent. of the total. The period covers weaning to mating. Pneumonia and enteritis were prominent with pneumonia taking precedence, and occurring as primary disease, in 27 per cent. and a further 12 per cent. had in addition diseases of other systems. Gross evidence of nephritis was present in approximately 10 per cent.

*Group 7 months to one year (117 cases)*

The number examined in this group represented 19 per cent. of the total. Neither enteritis nor enteritis complicated by pneumonia was seen. Pneumonia was present in 16 per cent. of cases compared with 39 per cent. in the previous age group. Does in this age group should have had 1 to 3 litters. Conditions associated with pregnancy and parturition occurred in 9 per cent., *e.g.* fur ball (impaction of the stomach with fur), metritis and mastitis. The incidence of nephritis as judged by gross lesions increased to 37 per cent. "Sore hocks," that is pressure necrosis of the bearing surfaces and the metatarsal region followed by ulceration, occurred in 10 per cent. with a secondary staphylococcal septicaemia in half the animals.

*Group one year and over (85 cases)*

The number examined represented 14 per cent. of the total. Nephritis was important with frequent gross lesions in 47 per cent. (40).

**Discussion**

Discussion can be best treated by dealing with the main groups of diseases under separate headings.

*Gastro-enteritis*

Enteritis, gastritis and caecal impaction featured in 30.4 per cent. of all examinations. Enteritis alone was present in 15 per cent. Lund (1951) found a total incidence of 49.8 per cent. in 3,210 rabbits over a period of three years. The first case examined was one week old. There was a sharp rise in incidence at 3 weeks when the nest box is left, reaching a sustained peak during the 5th, 6th and 7th weeks (see Fig. 2). A marked drop occurred between the 7th and 8th week with a second peak after weaning which faded with slight fluctuation to nothing at 5 months.

*Symptoms.* Generally all sick rabbits have a similar appearance. A rabbit suffering from gastro-enteritis loses its appetite, has a hunched-up appearance, diarrhoea of varying consistency, or constipation. Thirst is variable. The body temperature is frequently subnormal or normal.

*Post-mortem findings.* Rabbits dying with gastro-enteritis are not uncommonly in good body condition. If severe scouring has been a feature, faecal material may be caked around the animal's hind-

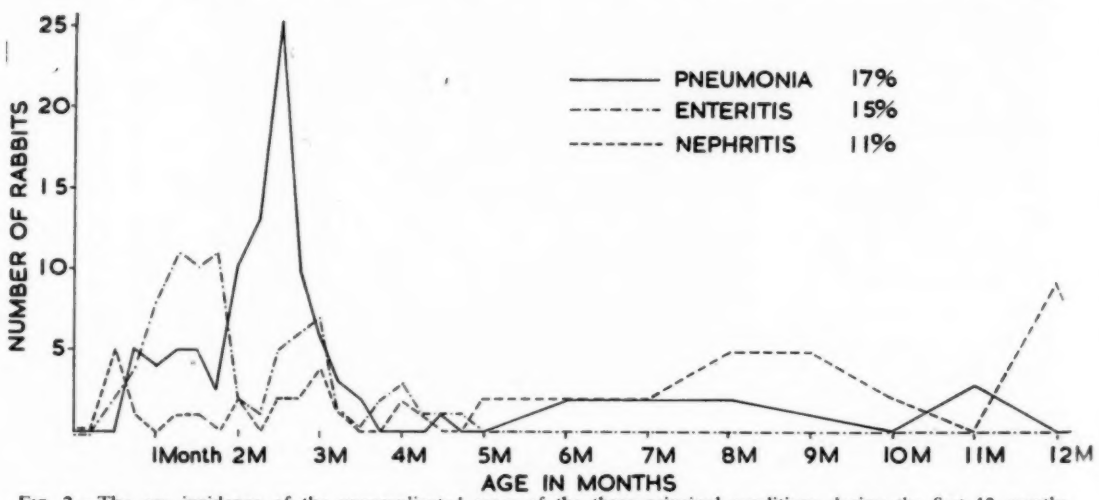


FIG. 2.—The age incidence of the uncomplicated cases of the three principal conditions during the first 12 months.

quarters. Blount (1957) states that a gastric catarrhal exudate is normally present an hour or so after death. Varying degrees of gastritis may occur as in other species. A striking and not common finding in a full stomach is haemorrhage into the gastric mucosa which is visible on the peritoneal surface as dark blotches or spots. Blount (1957) suggests a bacterial cause and Leontyuk (1959) a dietetic origin. Enteritis likewise may present a variety of tissue reaction and is commonly catarrhal, with an excess of fluid, or may be haemorrhagic or mucoid. The most striking features may be an haemorrhagic typhlitis or caecal impaction. Diffuse peritonitis with adhesions is not uncommon. The mesenteric lymph gland infrequently shows marked reaction.

Mucoid enteritis is a term frequently heard in relation to rabbit disease. Report (1949a) describes mucoid enteritis or so called bloat as occurring between 4 to 12 weeks, but also occasionally just prior to, or following, kindling. Diarrhoea may be a feature but often the first symptoms are anorexia, dullness, rough coat, intense thirst, tympanites and the passing of quantities of jelly-like mucoid material. The thirst increases and the animals appear to be in pain, sitting humped up over water while grinding their teeth. The temperature is usually subnormal. Does usually die overnight but the course often extends to 24 hours. The stomach is usually distended with an excess of mucus. The intestines may be empty or filled with varying amounts of fluid, varying in consistency from mucus to gelatinous material. In some cases the caecum may be impacted or distended with gas. Mucoid enteritis is said to be very common between 6 and 10 weeks (Blount, 1957). It is interesting to note that this overlaps the period during which gastro-enteritis was of highest incidence during the Survey. Diarrhoea of a mucoid consistency can occur in the terminal stages of intestinal coccidiosis (Chapman, 1929). Blount (1957) emphasises that diarrhoea is a feature of typhlitis and not of either intestinal or hepatic coccidiosis. The consistent presence of renal erosions in weaned rabbits is mentioned by Muir (1943) with urinary incontinence and loss of condition over several months in members of a litter that survived the acute stages of disease.

*Aetiology.* The aetiology of gastro-enteritis generally seems to be obscure and probably complex. Five workers—Blount (1957), Paterson (1956), Leontyuk (1959), Kurilov (1957) and Report (1949) consider that diet plays an important part. Kurilov (1957) observed heavy losses when early weaning was practised at 28 to 30 days as compared with 40 days. He related this to the gradual increase in stomach acidity and digestive ability which was expressed as 2.62 mm., at 25 days and 4.7 mm., at 40 days (the figures refer to Mett's test and are related to the length of digestion along a tube of egg-white by gastric pepsin). Rabbits weaned at 40 days showed a fall in stomach acidity and digestive ability which took 16 days to reach the pre-weaning level. This was thought to be partly due to the catarrhal reaction of the gastric mucosa to solid food. It was suggested that at 45 days old the rabbit is able to digest vegetable foods and by 3 months there was even better function. It is interesting to note that during the survey there was a marked drop in mortality due to enteritis from the 42nd day onwards. Leontyuk (1959) considered that most gastro-enteritis was caused by unsuitable food. The period of change from a diet of milk and solid food to one wholly solid was thought to be a time when any sudden change in diet constituents might be critical. He noted that gastro-enteritis reduced the level of absorption from the entire alimentary tract of the adult, but that it increased the rate of absorption from the stomach, duodenum and rectum of the rabbit aged 2 to 2½ months. The osmotic permeability of the whole of the intestines in adults is greatly reduced except in the duodenum and rectum, whereas it is increased in the whole intestine of the younger rabbit, particularly in the caecum, colon and rectum. These factors may explain the severe course and frequency of gastro-enteritis in the young rabbit. He also found by the use of fistulas that there was an increase in the amount of gastric and intestinal secretions during gastro-enteritis of all age groups. Gastric acidity is increased by as much as four times and intestinal alkalinity was depressed. There was a general and notable reduction in the digestion of protein and carbohydrates.

A study carried out over 15 years Report (1949b) on 18,829 suckling rabbits and using different combinations of cereal grains, plant protein supplements, vitamins, mineral matter, succulent foods, legumins and carbonaceous hay, led them to the conclusion that the kinds of foods used were not factors in preventing, causing, or curing enteritis. The same Department (1953) demonstrated that a variation of fibre in the diet between 12.1 per cent. and 20.8 per cent. did not lead to a significant difference in mortality.

The following experiences of the author suggest that a diet can be implicated in this country. It appeared to be associated with an outbreak of disease in a small rabbit unit of Californians with no previous disease problem. Within 48 hours of feeding a fresh consignment of pellets, scouring and deaths occurred in all ages. Death was not always preceded by scouring. Sick animals appeared to have an excessive thirst and died within 24 hours. Survivors grew very slowly. Two stud bucks in close contact rationed to 4 oz. of pellets daily were apparently unaffected throughout 4 to 5 weeks of the outbreak. Non-pregnant does and does in early pregnancy rationed to 6 oz. of pellets per day were also unaffected but consistently became ill as the food was increased to an *ad lib.* supply. Two young rabbits sold during the outbreak remained healthy and a litter of cross-bred rabbits folded on grass near the buildings, but not receiving pellets, remained healthy. On changing to another supply of pellets, death stopped within 48 hours, though the drug furazolidone at 0.4 per cent. was also supplied. On reverting to the original batch of food 2 weeks later, illness and deaths re-occurred within 48 hours and stopped as quickly on withdrawal. Altogether 40 out of 90 rabbits of all ages, but particularly those under two months, died during

4 to 5 weeks. *Post-mortem* examinations revealed consistent subacute enteritis with fluid intestinal contents. Non-haemolytic *Escherichia coli*, *Pasteurella* sp. and *Streptococcus* sp. organisms were isolated but not consistently. Hepatic and intestinal coccidiosis were not detectable. The standard of management, hygiene and housing was above average. The hutches were wire floored. The two foods were analysed. The main differences were 21.1 per cent. protein and 4.5 per cent. short cereal fibre in the food on which stock died, as compared with 14.4 per cent. protein and 13 per cent. long fibre in the food on which the rabbits thrived. The author realises the limited value of such analyses particularly as shortly afterwards it was found that 3- to 4-week-old rabbits on other premises were being fed pellets of the first formula and mortality was negligible.

The second rabbitry consisting mostly of Californians experienced scouring and death, particularly in 5- to 8-week-old rabbits. *Post-mortem* examinations revealed diffuse enteritis with fluid gastric and intestinal contents. Coccidiosis was not incriminated and bacteriological examination resulted in the consistent isolation of non haemolytic *E. coli* in varying numbers from all levels of the intestine. All ages of rabbits were divided into 3 groups and each group was fed a different pelleted food. Over a period of one month the group receiving the established food lost 19 young rabbits with symptoms as before, while the 2 groups receiving the other foods lost respectively one and none.

Apparently similar disease in another breeding unit was almost confined to suckling does and their litters. Stud bucks, growing rabbits, and does in early pregnancy were not affected, though frequently in adjoining cages. Chinchilla cross-bred does were more commonly affected than the New Zealand Whites and Californian breeds. Sometimes does were not observed to be ill but found dead, or they were obviously depressed, crouching by the water and died overnight. Scouring was not common. Some of the litters died before the doe, but usually at least one survived from a litter.

A consistent *post-mortem* feature was considerable fluid in the large and small intestines. Two does had a mass of transparent gelatinous material filling the large intestine. The caecum was commonly distended with gas. Slight pneumonia and hepatic coccidiosis were present in some, but parasitological and bacteriological results were not consistent. Thirty out of 200 does died during 2 to 3 weeks. A new batch of food had been introduced a few days before deaths commenced, and the deaths stopped following change to another food. As suckling rabbits may increase in weight by ½-lb. per week, this must represent a considerable milk production and thus food intake by the doe. It seems possible that this particular disease outbreak may have been a metabolic disturbance related to the actual amount of food consumed.

Mouldy hay appeared to be associated with the onset of scouring on another occasion.

It is not intended to imply that diet always plays a part in outbreaks of scouring or enteritis in rabbits, but as in other species, field observations suggest it is on occasion implicated in the multiple causation of disease. As the general livestock industry adopts increasingly intensive methods of production, the relationship between nutrition and health presents a fascinating and often perplexing study for the veterinarian in close co-operation with other workers.

During the survey non-haemolytic *E. coli* was commonly isolated from all levels of the intestine in cases of gastro-enteritis. The interpretation of these isolations was complicated as the animals had been dead for at least 24 hours. A relatively small number of isolates were untypeable with the usual range of sera. Further work is necessary to determine the rôle of *E. coli* as a rabbit pathogen.

*Clostridium welchii* infection was suspected in cases of haemorrhagic typhlitis but bacteriological examination never resulted in the isolation of the organism. Direct films of mucous membrane did, however, reveal many *Clostridium*-like rods in almost pure culture. Innes (1946) reports haemorrhagic typhlitis as a common *post-mortem* finding and suggests that *Clostridium welchii* may be responsible.

The isolation of *Salmonella typhimurium* from rabbits dying of acute disease has been reported by several workers. The clinical features of acute disease observed by Iyer and Uppal (1955-6) were anorexia, body temperature 104° F., soft faeces followed by diarrhoea and death in 24 hours. The *post-mortem* picture was of septicaemia. The spleen was usually enlarged 4 times and the Peyers patches were enlarged and obvious. Ghosh and Chatterjee (1960) observed haemorrhagic enteritis. Habermann and Williams (1959) observed focal necrosis of the liver and ulceration of the stomach and intestinal mucous membrane. Authors agree that the bacteria can be readily isolated in the acute phase. Heje, N-I (1958) could only isolate *S. typhimurium* from the intestine of 4 to 8 rabbits which were serologically positive. Morel (1958) isolated *Salmonella pullorum*. Habermann and Williams (1959) suggest that rabbits are resistant to infection with *Salmonella enteritidis*.

It is difficult to assess the rôle of coccidiosis in gastro-enteritis. Not uncommonly a few oocysts were present in the survey animals and it was considered that coccidiosis may have been a predisposing factor in some cases. Blount (1957) considered that scouring is not a feature of either hepatic or intestinal coccidiosis but is indicative of non-parasitic typhlitis.

The fungus *Sacchoromycopsis guttulatus* which is normally present in the intestinal tract of rabbits and other rodents has been incriminated in naturally occurring enteritis, Hage (1945). Death followed the oral administration of the fungus in spore and vegetative forms but the number of rabbits used was very small.

*Control and Treatment.* Gastro-enteritis appears to be as complex in the rabbit as in other species, and only broad measures of control can be applied until further research work has been carried out on its aetiology. It is possible that there may be a facet of management in individual rabbitries which could influence its incidence and course.

The U.S. Department of Agriculture (1955) describes a commercial fermentation product containing

2 g. chlortetracycline and 1.8 mg. of vitamin $B^{12}$ per lb., and other unknown substances which when mixed at the rate of 5 lb. per ton of food markedly reduced the mortality of unweaned rabbits to 3 per cent. when it was fed throughout the suckling period, as compared with 16 per cent. when it was only fed from the 36th to the 45th day after kindling. The weight of the litter at weaning was reduced probably because of the reduction in food palatability. Does required 7 to 10 days to become accustomed to the food. A reduction in the synthesis of vitamin $B^{12}$, riboflavin, niacin and pantothenic acid during the feeding of chlortetracycline was observed. Chlortetracycline, penicillin and a mixture of chlortetracycline, chloramphenicol and penicillin (Kurilov, Lipatova and Mashurko, 1958) were used on unweaned and weaned rabbits to assess their value in reducing mortality and improve growth rate. The unweaned group had access to oats, mixed fodder, oil cake, cooked potatoes, beet, hay and minerals. The results are presented in tabular form. (See tables III and IV.)

Apart from stating that scouring occurred in the control group of unweaned rabbits but not in the group receiving chlortetracycline, the clinical and *post-mortem* findings in the casualties were not reported. Chlortetracycline appeared to reduce mortality and improve the growth rate significantly.

TABLE III

SIX UNWEANED LITTERS FED ANTIBIOTICS BETWEEN 15 AND 40 DAYS OF AGE

| Dose per rabbit per day | Weight gain over controls at 40 days per cent. | Mortality at 40th day per cent. |
|---|---|---|
| Control ... ... ... | — | 18 |
| Penicillin 1 mg. ... ... | 18·8 | 7·1 |
| Chlortetracycline 0·5 mg. | 39·8 | 2·5 No scouring |
| Chlortetracycline 0·35 mg. Penicillin 0·65 mg. ... Chloramphenicol 0·65 mg. | 44·1 | 5 |

TABLE IV

FOUR GROUPS OF 39 RABBITS WEANED AT 40 DAYS AND FED ANTIBIOTICS UNTIL 90 DAYS OLD

| Doses per rabbit per day | Weight gain over control per cent. | Mortality by 3 months per cent. |
|---|---|---|
| Control ... ... ... | 0 | 33·3 Gastro enteritis a problem |
| Penicillin 2 mg. ... ... | 2·9 | 35 |
| Chlortetracycline 1 mg. ... | 16·1 | 0 |
| Chlortetracycline 0·35 mg. Penicillin 0·65 mg. ... Chloramphenicol 0·65 mg. | 5·3 | 13·5 |

Hills and Macdonald (1956) used chloramphenicol by intramuscular injection to control enteritis in artificially reared rabbits. The dose was not stated. Leontyuk (1959) suggested 0.1 to 0.3 gm. of chloramphenicol orally daily for diarrhoea while withholding food for 12 to 24 hours and administering alkaline and demulcent medicines.

Arrington and Davis (1958) said that nitrofurazone in the drinking water provided some control over enteritis but that this had not yet been fully evaluated. Sterility (Nissim, 1957) and weight loss (Pellerdy & Babos, 1952) are mentioned as side-effects of nitrofurazone therapy, but these were not observed by Macdonald (1957) who gave 50 mg. of furazolidone daily to does and 25 mg. to weaned rabbits who were also receiving drinking water saturated with nitrofurazone, containing 210 mg. per litre.

Hagen (1958) fed sulphaquinoxaline continuously in the food at the rate of 0.025 per cent. to 20 does and to their 367 unweaned young over a 12-month period. It had no effect on the incidence of enteritis as a whole but did reduce the incidence of haemorrhagic enteritis by 70 per cent.

Little can be done in the way of palliative treatment for animals that have been ill for a day or so. If they are observed in the early stages the withholding of water for 48 hours is suggested by Report 1949a), gradually re-introducing it over 5 to 7 days. A shortage of greenstuffs has been suggested as a causal factor and only succulent greens should be fed during the re-introduction of water. The placing of rabbits on a grass plot without food or water is said to be beneficial on occasions (Report, 1952). A reduction in the amount of food supply is recommended by Leontyuk (1959).

Glaubers salt (3 to 4 g. for young rabbits, 5 to 6 g. for adults), castor oil (1 to 1½ teaspoonfuls) or even a soapy enema are suggested treatments for constipation. Demulcent and alkaline drugs may be beneficial in all cases of gastro-intestinal upset and as a general principle, the diet should be slowly reintroduced over 5 to 6 days.

*Discussion.* The writer considers it is important to appreciate that the rabbit in the nest for 3 weeks is almost certain to acquire infection with hepatic and intestinal coccidiosis and possibly other diseases which may be established or incubating by the time the rabbit leaves the nest. Exposure to the general environmental conditions and an increasing food consumption may be factors of importance in the incidence of enteritis between 3 and 8 weeks. Several workers have stated that mucoid enteritis and enteritis are of highest incidence after weaning until three months of age. This is the period during which the young rabbit is adjusting itself to the common diseases and disturbances. There is evidence to suggest that the symptoms of enteritis and mucoid enteritis are sometimes related to a disturbance of the natural digestive processes. The fact that young rabbits and

suckling does are apparently particularly susceptible to disease of the gastro-intestinal tract could mean crippling economic loss. In view of the possible complex nature of the syndrome the approach can only be on general principles until further work has been carried out. The diseases of the gastro-intestinal tract of rabbits are to be shortly reviewed by Mack (1962). This fuller examination of the literature will probably permit a clearer picture of the problem.

2. *Respiratory Disease* (Synonyms: "snuffles," contagious catarrh, pasteurellosis)

Pneumonia was present in 27 per cent. of 600 carcases examined. It was present alone in 17 per cent. The earliest cases of pneumonia were seen in rabbits aged 2 to 3 weeks with the highest incidence at 10 weeks. Seventy per cent. of the apparently uncomplicated cases occurred in those aged 7 to 12 weeks (see Fig. 2). There was a higher incidence during the winter months but the practice of moving rabbits at weaning from a heated building to an unheated one with corrugated iron roof, and fluctuations of environmental temperature may have provided an important predisposing factor in this particular unit. Lund (1951) found pneumonia in 22.7 per cent. of 3,210 rabbits. The age and percentage incidence is compared in Table V.

TABLE V

AGE AND PERCENTAGE INCIDENCE OF RESPIRATORY DISEASE

| Age groups | Lund | | Ostler | |
|---|---|---|---|---|
| | Per cent. | Number | Per cent. | Number |
| 0 to 3 weeks ... | 11·4 | 86 | 0 Very few examined in this group | 0 |
| 4 to 8 weeks ... | 58·4 | 443 | 30 | 47 |
| 9 weeks to 6 months | 13·2 | 104 | 55 | 86 |
| 7 months to 1 year and over... ... | 17 | 127 | 15 | 24 |

The total incidence is not significantly different, and it is likely that the different incidence between the age groups of the two surveys may be partly attributable to different management.

*Symptoms.* In acute cases there may be only slight premonitory symptoms, the animals usually being found dead. In less acute cases the first symptom may be frequent sneezing followed by nasal discharge, and ocular discharge which may lead to loss of fur below the eye; depression, laboured breathing and possible diarrhoea. The course of the disease may be extended or death may occur between 2 to 7 days.

*Post-mortem* findings. Usually the anterior portion of each lung is involved, up to 75 per cent. of the lung tissue being affected. The pneumonic tissue is firm, deep red, and clearly demarcated from the remaining lung. It is often possible to express creamy pus from the bronchioles on the cut surfaces. Pleurisy, pericarditis and some empyema can occur. Peracute tracheitis with froth in the lumen, and rhinitis are usually present. Bacteriological examination was carried out in 153 cases of pneumonia during the survey. The following isolations were made:—

| | |
|---|---|
| Coliform organisms (pure culture) ... ... | 69 |
| Coliform organisms (with other bacteria) ... | 18 |
| *Streptococcus* sp. organisms (pure culture) | 13 |
| *Staphylococcus* sp. organisms (pure culture) | 12 |
| *Pasteurella* sp. organisms (pure culture) ... | 7 |
| *Pasteurella* sp. organisms (with other bacteria) ... ... ... ... | 12 |
| *Haemophilus* bronchisepticus (pure culture) | 9 |
| Culture sterile ... ... ... ... | 28 |

Hagen (1953) describes the lesions seen in this survey and gives a comprehensive list of references. He studied the incidence of respiratory diseases in 45 does, when 5 out of 45 does and 35 out of 857 of their progeny died as the result of pneumonia. *Pasteurella multicoida* was isolated from each of the does, and from 54 per cent. of the young rabbits which died. *Haemophilus bronchisepticus* from 28.5 per cent.; and *Micrococcus pyogenes* from 17.2 per cent. *Mycobacterium* sp. organisms and fungi were never isolated. Very little histopathological examination appears to have been carried out.

*Aetiology.* Very little detailed work has been carried out to elucidate the aetiology of enzootic pneumonia and it seems possible that the bacterial isolations may represent secondary infection following a primary virus or protozoon disease.

In examining a selection of these rabbit lungs from this survey microscopically, MacKenzie (1961) observed that the histological changes principally suggested a tissue reaction to bacterial invasion. Lesions in some affected lungs, however, particularly in adults, suggested the possibility that a proliferative virus-type pneumonia might also be implicated. Demonstration of an experimentally transmissible non-bacterial pneumonia from these cases has not so far been attempted. Histological examination of the nasal structures from two young rabbits in the very early stages of rhinitis or "snuffles" revealed only a lymphocytic reaction.

Hagen (1953) suggests that does transmit infection to their litters within a few days of birth. It is probable that a high percentage of adult rabbits carry *Pasteurella* sp. organisms in the respiratory tract. Paterson (1956) considers that pneumonia is probably aggravated by pregnancy, parturition, and heavy lactation which leads to heavy losses in the breeding stock and that poor environment conditions may account for pneumonia reaching epidemic proportions in some young stock. The distribution of gross *post-mortem* lesions resembles those in so-called virus pneumonia of pigs, being mainly confined to the anterior lobes of the lungs.

*Control.* One producer, breeding New Zealand Whites, maintains that respiratory disease is not a problem when buildings have open sides above rabbit level. This may not apply elsewhere with other breeds and strains, but with the present state of knowledge it would seem better for the industry to accept an increased food consumption possibly caused by lower

environmental temperatures, if it is not a critical economic factor. Paterson (1956) has suggested an ambient temperature of 50°F., but the writer is not aware of any guiding figures for optimal humidity.

Vaccination against pasteurellosis in rabbits has always given controversial results, vaccination protecting one group but having no value in another. A mixed vaccine containing *Haemophilus bronchisepticus, Pasteurella septica* and *Staphylococcus albus* was reported to be of value in 90 per cent. of outbreaks by Meek (1943).

During the survey a trial was undertaken to evaluate the effectiveness of an autogenous formalised whole broth culture *Pasteurella septica* vaccine. Half-litters were vaccinated subcutaneously with 1 ml. at 6 weeks and 8 weeks of age. Agglutination tests were performed on the serum of the 12 control and 12 vaccinated animals, using an antigen prepared from the vaccine culture. The vaccinated rabbits had received the second dose of vaccine at least a month previously. Of the vaccinated group 10 had a titre of 1:20 and 2 of 1:40. Of the control group 7 had no titre, 4 had 1:20 and 1 of 1:40. The incidence of pneumonia as judged by the number of casualties was not significantly affected by vaccination. The serological results of the above trial have, however, prompted a second trial using a vaccine containing *Haemophilus bronchisepticus, Pasteurella septica* and *Staphyloccus aureus*.

*Treatment*. Ventilation with its effect on the ammonia concentration as well as the humidity of the atmosphere may be of prime importance.

Aerosols can provide a high vapour concentration which may be of value in palliative and therapeutic treatment during an outbreak of respiratory disease. Several rabbitries where rhinitis (" snuffles ") has been prevalent have reported an apparently beneficial effect following the use of a medicated aerosol generated by a Microsol machine.

Huygelen (1958) reported that dihydrostreptomycin administered subcutaneously at the rate of 100 mg. per kg. bodyweight repeated on 3 successive days controlled an outbreak of pasteurellosis. The necessity for complete disinfection at the start of treatment was emphasised. Oxytetracycline at the rate of 0.4 per cent. in the food for 7 days was shown to be effective if chronic cases were destroyed and disinfection was adequate. Chlortetracycline was less effective. Oxytetracycline and dihydrostreptomycin were not effective in severely affected chronic cases.

Sulphaquinoxaline and furazolidone were evaluated by Hagen (1959). Sulphaquinoxaline at the rate of 0.025 per cent. in the pelleted food was fed to 20 does and their unweaned young for 12 months. There were no cases of primary pneumonia, but 8 secondary cases, as compared with 11 primary cases and 7 secondary cases in the control group. The feeding of sulphaquinoxaline reduced the recovery of *Pasteurella* sp. organisms by 50 per cent. The food was palatable and non-toxic. Furazolidone in the pelleted food at the rate of 0.0055 per cent. gave 9 cases of primary and 7 cases of secondary pneumonia as against 14 cases of secondary in the control group. The food was palatable and non-toxic.

3. *Coccidiosis*

A review by Davies, Joyner and Kendall (1961) was freely consulted in the preparation of this section. Coccidiosis is a severe disease of young rabbits and can be divided into hepatic and intestinal forms.

*Hepatic coccidiosis*. This is caused by one of the most pathogenic coccidia of rabbits, *E. steidae* and may cause a high rate of mortality. There is a difference of opinion on the incidence of the disease. Davies *et al*. (1961) suggest that it is not as common as the intestinal forms. Lund (1951) working in the U.S.A. found a low incidence. MacDonald (1957) working in Great Britain and using a histological criterion was unable to obtain rabbits free from infection from any dealers over a wide area but found a low incidence in a small amount of material from the Continent. It is generally accepted in the trade as being a common disease in rabbits kept on solid floors. One dealer slaughtering rabbits from a small area reported condemnation of livers from 20 out of 30 premises. The coccidia multiply in the epithelium of the bile ducts which became distended with white/yellow material that usually contains myriads of oocysts. The sporulation time is approximately 58 hours and the pre-patent period 15 to 16 days with a peak of oocyst production at around the 23rd day, falling to the 37th day when very few oocysts can be detected. Considerable immunity follows even a light experimental infection and usually there is little reaction following challenge, whereas control rabbits die 6 weeks later.

*Symptoms*. There are only slight symptoms during the pre-patent period, after which the appetite decreases with loss of condition, pot belly, and death approximately 5 weeks after infection. In less severe cases the animal may appear unaffected. Bull (1958) found the highest incidence in the wild rabbit from 6 to 11 weeks of age, it is interesting to note that this age overlaps the period during which enteritis was at a peak during the survey.

*Diagnosis*. The demonstration of oocysts in the faeces, as in other species, is not a firm foundation for believing that an animal is suffering from coccidiosis (Horton-Smith, 1958). *Post-mortem* examination will reveal the typically enlarged liver with distended bile ducts appearing as yellow/white marks. Oocysts in the gall bladder will be those of *E. steidae*.

*Treatment*. The sulphonamide drugs are of value. Sulphaguanidine is reported to be of value by Joshua (1943) at the rate of 0.5 mg. per kg. in mash on 2 successive days, but toxicity has been reported. Sulphadimidine at 0.5 to 1 per cent. or sulphaquinoxaline at 0.1 per cent. in the food and water continuously for 14 days are recommended by Horton-Smith (1958).

A 0.2 per cent. solution of sulphadimidine was used continuously in the drinking water for up to 24 days by Davies *et al*. (1961). He recommends a sulphonamide for 2 to 10 days to all rabbits following diagnosis of coccidiosis and a second course 7 days later.

*Control.* Davies *et al.* (1961) emphasise the need to rear rabbits under clean conditions to ensure that the rate of oocyst intake is low. During the course of the survey only one adult rabbit had macroscopical evidence of hepatic coccidiosis, being from a rabbitry where all the rabbits were kept on wire and a coccidiostat was not fed. Sulphaquinoxaline at 0.025 per cent. is the coccidiostat commonly incorporated in pellets. A saturated solution of nitrofurazone containing 210 mg. per litre was used effectively by Macdonald (1957), but the animals were isolated from other stock. Hagen (1961) did not obtain effective control when using nitrofurazone at 0.011 per cent. in the food.

If hepatic coccidiosis causes lesions visible to the naked eye the liver is unsaleable for human consumption. As the organ weighs approximately 4 oz. this would represent considerable economic loss. At the moment the livers are condemned irrespective of their condition but this may not always be the case. Therefore, ideally, a coccidiostat should not only control mortality but also the disfiguring bile duct lesions.

*Intestinal Coccidiosis.* Four species of *Eimeira* parasitise the main intestine and can be differentiated microscopically into *E. media, E. perforans, E. magna* and *E. irresidua.* The latter 2 are considered to be more pathogenic. Kessel and Jankiewicz (1931) consider that the minimum sporulation time for the different species varies between 30 and 50 hours, hence the need for daily removal of faeces and the advantage of clean wire mesh floors. The time taken for a complete life cycle varies from 5 to 9 days. *E. irresidua* causes the most severe tissue reaction and patches of epithelium slough away from the intestinal wall. The probable pathological effects are disturbed nutrition due to mechanical damage and there may be toxic absorption following tissue necrosis. Resistance to infection by *E. perforans* has been demonstrated by Bachman (1930). It seems likely that the coccidial species are not closely related antigenically.

*Symptoms.* Blount (1957) stresses the absence of diarrhoea in intestinal coccidiosis. Chapman (1929) found over 50 per cent. of affected rabbits died with no premonitory symptoms except severe diarrhoea which in 70 per cent. of cases did not occur until 24 hours before death and the animals were previously clinically normal. Initially the scouring was profuse and watery, later becoming mucoid. An affected rabbit is depressed, refuses food and may have an excessive thirst. Blount (1957) observed a loss of condition, staring coat and anaemia.

*Post-mortem features.* Chapman (1929) described distension of the duodenum the contents varying from a chalky-white colour to transparent mucus. Petechial haemorrhages were common in the caecum with watery or mucoid contents. Microscopically ulceration was obvious being more predominant in the duodenum. Blount (1957) described elongated, honeycomb slate-grey markings outlined by pink blood vessels as being characteristic of coccidiosis.

*Treatment.* There is little information available. Davies *et al.* (1961) suggest that a soluble sulphonamide used as in the hepatic form would probably be of value. 0.5 g. of sulphamerazine orally twice daily for 2 days and sulphaquinoxaline in food or water at 0.1 per cent. for 14 days has proved effective (Horton-Smith, 1958). 0.5 to 1.0 g. per kg. of nitrofurazone for prevention and 1.5 to 2.0 g. per kg. for treatment prevented large losses and considerably reduced the oocysts excretion. The coccidial species were not stated (Boch, 1957).

*Prophylaxis.* During the course of the survey intestinal coccidiosis was suspected in young rabbits which had died during scouring. Though oocysts were commonly present in films of intestinal mucosa, limited material examined histologically did not reveal severe tissue damage. Gross lesions of intestinal coccidiosis were not seen in any of the carcases during the survey, and as a coccidiostat was not fed at any time it seems probable that wire mesh floors kept clean offer a useful method of control. There may be occasional clinical cases, or the level of infection may possibly cause sufficient damage to precipitate scouring following secondary bacterial multiplication. It will be remembered that non-haemolytic *E. coli* was commonly recovered from all levels of the intestines in animals which had died scouring. In the control of both hepatic and intestinal forms it is important to maintain a high standard of hygiene, measures being taken to prevent faecal contamination of the food, water and fur. Sulphaquinoxaline, which is commonly used as a coccidiostat in the food when solid floors are in use, appears to be of value in the control of clinical diseases as judged by field evidence. If a coccidiostat is administered continuously the rabbits may remain fully susceptible to the disease. This factor should be borne in mind when purchasing new stock. Basic research is needed into the control of coccidiosis. The losses and any reduction in growth rate due to this disease will become increasingly important as the industry develops.

4. *Nephritis*

Nephritis was the third most common condition observed. It was seen in a total of 23.2 per cent. of all carcases. In 11.2 per cent. it was the only *post-mortem* finding. The earlier cases occurred at 2½ weeks but it occurred in all age groups (see Fig. 2) and it was rare not to find lesions in rabbits of over one year old. Albuminuria was common. Lund (1951) does not mention nephritis. Blount (1957) draws attention to the high percentage of rabbits with albuminura and nephrosis. Nephritis, identified by cortical pitting, was commonly observed by Ford (1943) during the *post-mortem* examination of 1,000 rabbits from all parts of Britain in 1943.

*Symptoms.* No symptoms may be detectable in the acute stage though it is suggested that torticollis or paraplegia may occur. In advanced cases there is a marked loss of condition, even approaching emaciation. Terminal diarrhoea and matting of the fur of the hindquarters, with localised wet eczema may occur. The control of balance may appear to be disturbed.

*Post-mortem features.* The most striking acute lesions were seen in a group of 8-week-old New Zealand White bucks condemned as unfit for human consumption. The flesh was congested, badly set, and the carcases were below average weight. The kidneys were 2 and 3 times the normal size and softer than usual. Circumscribed, irregular grey areas were diffusely distributed over the cortices of both kidneys. The carcase lymph glands were enlarged and oedematous. The kidneys in affected rabbits over four months of age, have obvious depressions or pits in the cortices which often seem to be concentrated at the poles (Fig. 3). The centre of the pit is usually pale with what appears to be a surrounding zone of hyperaemia. The number of pits usually increased with age, when an obvious irregularity of the surface occurs. In advanced cases the kidneys are gnarled, irregular balls of fibrous tissue and the carcases are emaciated. The gross appearance of the urine can be misleading as a heavy precipitate of phosphates appears to be normal. When albuminuria is present, the urine is frequently pale and clear. Ten per cent. of the carcases showing chronic nephritis had fur ball impaction of the stomach which may possibly indicate a depraved appetite.

*Histopathology.* This will be dealt with in greater detail (Ostler & Lancaster). The pale areas in the kidneys described above are related to massive infiltration with lymphocytes. Later cases are typified by the destruction of the tubules with cicatrical contraction, causing cortical pitting. Glomeruli appeared to be involved only if they are adjacent to tubular damage, *i.e.*, the condition is primarily a nephrosis. In chronic cases fibrous replacement is striking. Minute elongated rods approximately 1.5 x 0.5 micron with darkly staining nuclei were demonstrated lying free in groups in the lumen of tubules (Fig. 4). Perivascular cuffing with lymphocytes was observed in the brain tissue together with an infiltration of the meninges with lymphocytes. One doe which was described as "silly" before death had marked perivascular cuffing in the cerebrum as well as a severe nephrosis. Identical gross and histological kidney lesions have been seen in individual rabbits from eight other unrelated rabbitries.

*Aetiology.* During the survey, aerobic and anaerobic bacteriological examination of visibly affected kidneys did not give any consistent results and usually the tissue was sterile. Examinations for leptospirosis both by direct microscopy and culture, were negative. The examination of seven blood samples for blood urea gave a range from 30 mg. per 100 ml. when the kidney was lightly pitted and of normal size, to 60 mg. per 100 ml. when the organ was fibrosed, contracted and pale. A limited number of haematological examinations gave results within the wide normal range of the species. Lancaster (1961) observed organisms resembling *Toxoplasma gondii* in typically pitted kidneys and subsequently this observation was confirmed on several occasions. A random group of blood samples was subjected to the complement fixation test for toxoplasmosis and 10 out of 58 were positive.

Havlik and Hubner (1956) found serological evidence of toxoplasmosis in 104 out of 110 rabbits from 10 sources. Moller (1958) found *T. gondii* in 1 per cent. of rabbit carcases from 23 herds, using histological and biological methods of demonstration. He also isolated the organism from a sample of pooled muscle. Hudson (1956) demonstrated *T. gondii* in rabbit brain. Beverley, Beattie & Roseman (1954) demonstrated a high level of antibody production to *T. gondii* in rabbit trappers, but suggested that toxoplasmosis is a commensal relationship. However, outbreaks of disease in rabbits have been associated with the protozoan by Thompson and Worden (1956).

Yost (1958) described a mild chronic disease of rabbits with no pathogenic features, in which chronic nephritis with pitting of the cortex due to fibrosis of the tubules was a common feature. Granulomata of the brain, myocarditis and parametritis, were also observed. Albinos were said to be more susceptible than coloured rabbits. *Encephalitozoon cuniculi* which is a protozoan parasite, closely resembling *T. gondii*, was isolated biologically using white mice. *E. cuniculi* was first described by Wright and Craighead (1922) as being responsible for paralysis in young rabbits. They observed lesions in the brain, liver, spleen, kidney and myocardium. Grey spots were present on the surface of the kidneys. No organisms could be demonstrated in the kidney during the acute phase. Goodpasture (1924) also found small grey kidney lesions when describing a spontaneous encephalitis in rabbits and found lesions in the brain, kidney and lungs.

The causal agent of the particular nephritis seen in this survey is not clear. Either *T. gondii* or *Encephalitozoon cuniculi*, or both may be responsible. Differentiation of the parasites is difficult and at the moment appears to rest largely on selective staining methods. Olafson and Monlux (1942) suggested that the organisms are identical. Wolf, Cowen & Paige (1939) accepted that there were 2 types of organisms but stressed the need for further work on differentiation. There is no specific serological test for *E. cuniculi* and there is said not to be any significant cross-reaction between the 2 organisms. The results of the complement fixation test for toxoplasmosis suggested a lower level of infection than might have been expected if the kidney lesions were solely due to that disease.

Nephritis appears to be a common disease of rabbits and is probably the salient *post-mortem* feature of a generalised infection. Goodpasture (1924) considered the disease he described to be highly contagious by contact and from urine. As nephritis is a chronic disease occurring in all age groups, opportunity for transmission may occur *in utero*, during suckling following fostering, during the rearing of mixed litters, in colonies and during mating. It seems probable, therefore, that the disease has ample opportunity to spread through a rabbitry. A reduction in the growth rate of the meat rabbit during the acute phase of disease together with a reduction in the life span of breeding does and the effect of chronic disease on the course of concomitant infections, may prove important economic factors in an industry operating on a narrow margin of profit.

*Control and Treatment.* Nephritis is a chronic disease of indefinite aetiology and the excretion of the causal organisms in urine may occur throughout life. Adequate serological tests which could be used as a basis for eradication are not yet available. In the present state of knowledge one approach for control might be to use a combination of the serological examination of virgin does at mating for evidence of toxoplasmosis, combined with the histological examination for evidence of nephritis in members of resulting litters. Bucks and does remaining from litters apparently free of disease could then be reared for continued testing.

Therapeutic treatment, possible vaccination, public health aspects and possible transmission of infection to other farm animals cannot be usefully considered until the aetiology of nephritis in rabbits is definitely established.

4. *Other conditions which were seen or suspected*

*Pregnancy toxaemia* was suspected. It is said to be fairly common in the later stages of pregnancy (Greene, 1937-38).

*Hypocalcaemia* was suspected but not confirmed.

*Mastitis.* Only 5 cases were seen and *Staphylococcus* sp. organisms were isolated which were sensitive to all the common antibiotics.

*Ear Canker.* The causal agent is the mite *Chorioptes cuniculi* which was seen in brown ear discharge on several occasions. Two adults had a permanently rotated head due to secondary middle-ear disease. *Psoroptes communis* can also be responsible. Treatment consists of softening the discharge with oil and introducing a suitable parasitic dressing. Thorough disinfection of the accommodation is desirable.

*Malocclusion* is said to be inherited. The continuously growing incisors do not meet against each other through poor apposition, prehension is difficult, buccal damage may occur and the animal may eventually starve. A tattered appearance of the fur is produced by an affected animal grooming itself. Culling is desirable.

*Overgrown nails.* To prevent this, nails are commonly clipped at mating.

*Splay leg* is a descriptive term which applies to the positioning of the hind legs which become twisted laterally. Innes and O'Steen (1957) consider the disease to be an inherited osteoarthopathic dysplasia of the hip and shoulder joints analogous to that in dogs and in children. Rickets is rare in rabbits.

*Sore Hocks.* This is a pressure necrosis of the skin over the plantar surface of the metarsal bones causing a bilateral circumscribed area of acute inflammation (Fig. 5). In severely affected cases secondary infection with *Staphylococcus aureus* may occur and arthritis may be present in all four limbs. A generalised infection with embolic abscesses in the kidneys is not uncommon. It appears to be a condition primarily associated with wire floors and is relatively uncommon on well bedded dry floors. Vaida (1959) considered the irritant action of ammonia from urine sodden bedding to be a predisposing factor. He obtained good healing by providing adequate dry bedding combined with local treatment with a 0.2 per cent. solution of aluminium acetate. An indestructible resting board such as asbestos may be of prophylactic value. Antibiotic treatment is indicated.

5. *Some other conditions which have been reported.*

*Infertility.* This has been associated with infection by *Pasteurella septica* or *Haemophylus bronchisepticus* following severe attacks of snuffles (Kyaw, 1945). The bacteria were isolated from the uterine contents and penile swabs.

*Pseudo tuberculosis* (caused by *Pasteurella pseudo tuberculosis rodentium*). This is a common disease of wild rodents. There is a progressive loss of condition. Caseous nodules in the intestinal wall and later in the mesenteric lymph gland, spleen and liver can be seen on *post-mortem* examination. Infection is transmitted through faeces and the slaughter of the mother, litter mates, and any animal in poor condition is desirable.

*Tuberculosis.* The rabbit is susceptible to the bovine and avian strains, but the disease is rarely seen.

*Listeriosis.* Abortion, stillbirth and pyometra have been attributed to *L. monocytogenes* infection. An epizootic form in young rabbits has been reported.

*Fusiformis necrophorus infection* (Schmorl's disease). A normal inhabitant of the rabbit skin this organism is commonly involved in secondary infection of wounds. Necrosis of the lips has also been reported. Generalisation of the infection is not uncommon. Any wound should be treated and any animal with a skin abscess is better culled.

*Myxomatosis* (Thompson & Darbyshire, 1961). The virus disease was first reported to be present in wild young rabbits in Great Britain in 1953, and is highly specific for the species belonging to the genus *Orcytolagus*. It can be transmitted by direct contact mechanically and by the European flea *Spilopsyllus cuniculi*.

Fleas may be present in hundreds on a rabbit and remain infected from 5 to 7 days after a blood feed. The incubation period of the disease is 5 to 7 days, after which there is a clear watery discharge from the eyes; the discharge thickens in 1 to 2 days, eyelids swell, become very limp and adhere, with a tenacious inspissated purulent exude, followed by swelling on the nose and muzzle and other parts of the body. Death occurs 11 to 18 days after infection.

The virus and a closely related fibroma virus are both members of the pox-virus group. Rabbits which recover from a fibromatosis infection often possess a good immunity against myxomatosis. Such animals when challenged may either completely resist infection, develop a mild infection or succumb to generalised myxomatosis.

The strain of fibrom virus used for vaccination is important and intradermal inoculation is more effective than the subcutaneous route. It is unsafe to vaccinate rabbits under one week of age but there is less risk in the second week if the doe has herself been previously vaccinated. The immunity of the doe does not affect the development of immunity in the young. Fibromatosis offers a good measure of pro-

tection against myxomatosis and should be repeated every six months.

In commercial rabbit-keeping, myxomatosis is unlikely to be a serious hazard if there is no opportunity for direct contact with wild rabbits and the rabbit flea vector. One case was reported where the hutch was kept on ground level (Spence, 1961). Rabbit houses should therefore be completely stock-proof.

*Rabbit pox.* A highly contagious and fatal disease (Greene, 1934-5; Rosahn & Hu, 1935) has occurred in U.S.A. The symptoms vary but macular and pustular lesions commonly occur especially on the ears and buccal mucous membrane.

*Exanthema.* A fatal disease probably caused by a virus (Raspini, South America, 1957) was characterised by exanthema of the lips, mouth and face. Vaccination was of value.

*Rabbit syphilis.* Caused by a spirochaete, *Treponema cuniculi*, this condition is said to be relatively common (Middleton, 1932). It is harmless to man, and to other domesticated animals. Papules occur on the skin of the external genitalia which develop to weeping ulcers. Infection may spread to the hocks and head, and generalisation may occasionally occur, when mange might be suspected. Lesions in young rabbits can cause difficult micturition and defaecation. Neosalvarsan and the antibiotics can be used for treatment. Disinfection should be thorough.

*Body mange.* It can be caused by the mites *Sarcoptes cuniculi* and *Notoedres cuniculi*, but is relatively rare. Yellow to grey scabs develop on the head parts causing intense irritation. Culling is desirable.

*Ringworm.* *Microsporon audouini* infection has been reported by Ravaioli and Tonolo (1956). Circular areas denuded of hair are a feature. Culling is desirable.

*Parasitic gastro-enteritis.* A round worm *Graphidium strigosum* found principally in the stomach but also in the intestine can cause diarrhoea and emaciation. A high worm egg count is diagnostic. Piperizine might be tried. *Passalurus ambiguosum*, resident in the caecum and colon is generally considered non-pathogenic but Holmes (1961) reported having found it in very large numbers where scouring was a problem. Poor hygiene is usually contributory to worm infestation.

*Bladder worms.* *Cysticercus pisiformis*, the larval form of the dog tape worm *Taenia pisiformis*, and *Coernurus serilias*, the larval form of the dog tape worm *Taenia seriolis* are both found. Severe infestation with *Cysticercus pisiformis* and migration through the liver with cystic development in the peritoneum can cause unthriftiness in young rabbits and abdominal distension in the adult. *Coenurus serilias* develops subcutaneously. It is non pathogenic and can be removed surgically. Contamination of rabbit food by dog faeces should be avoided at all times.

## General Discussion

In considering the prevention and the control of the diseases of any species it is obviously important to relate all the recommendations to the system of husbandry. This is of extreme importance when intensive methods of production are applied. Each disease subject has been discussed in context but the writer would like to emphasise that in broiler rabbit production, disease occurs in a system where the stock is concentrated in close confines, possibly under one roof, provided with an artificial environment, often fed solely on a processed food, mated at an early age and kept more or less continually pregnant.

Diseases of the alimentary and respiratory tracts together with nephritis, caused the majority of ill health and deaths in this rabbitry and are subjects in need of thorough investigation.

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### The Speaker's Introduction

**The Chairman, Mr. H. A. Crawshaw,** said it was a pleasure to introduce Mr. D. C. Ostler from the Veterinary Investigation Centre at Reading. For a long time Mr. Ostler had been interested in the poultry industry and the troubles associated with poultry, and naturally he then turned to the diseases of broiler rabbits. The word "broiler" appeared to be a little unfortunate, and it was a shame that the word had been copied from the chicken industry. However, Mr. Ostler had made a study of rabbits, and the Association were grateful to him for attending the Congress to give members the benefit of his advice on a subject which was becoming more and more important.

**Mr. D. C. Ostler** said that his paper might have been more accurately entitled "The husbandry and some hazards of commercial rabbit production." The husbandry had been dealt with in some detail because it would probably be agreed that in considering the diseases of animals kept in an intensive system, it was essential to grasp the fundamentals of the husbandry methods to form a general background. The preamble therefore was intended to assist the practitioner faced for the first time with a disease problem in a commercial rabbitry, particularly where an error or factor of management was implicated.

The results of the examination of approximately 600 rabbits from one large rabbitry over a period of 18 months was used as a basis for discussing the disease hazards. The rabbitry was established a few years ago with New Zealand White breeding stock purchased from the continent and the United States. It was possible that variations in the management, breeds, sources of foundation stock and genetic differences might well influence the disease pattern in other rabbitries.

The first 3 weeks of the rabbit's life were normally spent in the nest where it was in intimate contact with the doe and her bacterial, viral and parasitic flora, but it was protected from the general environment of the rabbitry during the suckling period. Very few animals were examined *post-mortem* between birth and 3 weeks of age and losses might be higher than was suggested. At 3 weeks of age the rabbits normally left the nest and were almost certainly infected with coccidiosis and, possibly, other disease agents. They were then subjected to the general environmental conditions and started to eat solid food.

The rabbits were weaned at 8 weeks, but some rabbitries practised weaning at 3½ to 4 weeks. The majority of deaths occurred between 3 weeks and 3 months of age and enteritis and pneumonia predominated. It was suggested that adjustment to the environmental factors, solid food and the presence of subclinical disease was of importance in influencing the mortality and the morbidity rate during that period. At 3 months of age the mortality rate dropped to a lower level which remained almost constant.

The principal *post-mortem* features had been grouped into gastro-enteritis, pneumonia and nephritis.

Gastro-enteritis almost certainly represented a disease complex. Physiological factors related to age appeared to be important to the incidence in the unweaned and recently weaned rabbit, as the Russian workers had suggested, and rabbits weaned over 40 days of age were more able to digest solid food than those weaned at 28 to 30 days. It was difficult to assess the rôle of nutritional factors in the incidence of gastro-enteritis in rabbits of all ages.

The importance of the percentage of fibre in the diet was open to doubt, as he had recently heard of a diet containing 3 per cent. fibre which produced negligible mortality when fed to recently weaned rabbits. *Escherichia coli* was commonly islated from all levels of the intestinal tract when enteritis was present and it did not appear to be a normal inhabitant of the intestinal tract, but its rôle as a pathogen was not clear. It seemed possible that a low level of coccidiosis might predispose towards bacterial enteritis.

There seemed little justification for attempting to subdivide the complex and speak of mucoid enteritis as though it was an entity. Gastro-enteritis might only occur in a few rabbits, or it might be a severe problem resulting in considerable economic loss and an unsatisfactory response to medication.

Pneumonia occurred from a few weeks of age onwards, but reached a peak soon after weaning at 8 weeks. As in other intensively kept species, ventilation was probably an important factor influencing the incidence and the course of respiratory disease. There was evidence to show a lower incidence with free ventilation and the rabbit did not appear to suffer ill effects from the low environmental temperature. The relationship between the commonly occurring rhinitis or "snuffles" and pneumonia was not clear, but there was some evidence to suggest that a virus infection might be involved.

Not uncommonly pneumonia and nephritis occurred together, and it seemed possible that one might predispose towards the other. No bacterial species was consistently isolated and one wondered whether bacteria played a primary or secondary rôle.

Two workers had already noted a high incidence of

nephritis in the British rabbit population. A large number of kidneys from mature rabbits in the colony under study had gross evidence of chronic nephritis and lesions thought to represent the acute phase were seen in a few 10-week-old rabbits.

It was suggested that the gross kidney pitting indicated the chronic stage of an acute generalised infection, possibly contracted from the doe during the suckling period, survivors themselves becoming carriers. It was further suggested that the central nervous system might be involved during the acute phase, causing paraplegia or partial rotation of the head; but insufficient work had been done to justify associating nephritis with any other lesions or symptoms. The literature suggested that infection with *Encephalitzoon cuniculi* could produce such lesions. Serological tests indicated a significant infection with *Toxoplasma* so that both these organisms might be present, and morphologically it was difficult to differentiate between them.

At the present stage he felt it could only be said that nephritis, as indicated by pitting of the cortex, was relatively common and if severe enough could cause unthriftiness. The aetiology however was indefinite.

Coccidiosis was one of the hazards of intensive rabbit production. The majority of rabbits appeared to carry a low level of infection, but if they were reared on wire floors which were kept clean or a coccidiostat was administered continuously combined with good hygiene, the morbidity and mortality levels appeared to be low. Disfiguring hepatic lesions occurred to a varying degree under both systems and necessitated condemnation of the organ for human consumption. Little research work had been carried out on the disease.

A limited number of other conditions had been briefly mentioned in the paper. It should be remembered that the rabbit had been used intensively as a laboratory animal and data regarding the species was scattered through the scientific literature. An attempt was being made to correlate that information which was spread over at least 20,000 to 30,000 references.

The rabbit was able to utilise waste vegetable matter. By such conversion it offered a means of raising the pitifully low animal protein consumption in the underdeveloped countries. Any research into the control and treatment of rabbit disease would not only assist the rapidly developing industry, but might indirectly affect the health of other less fortunate populations.

It was plain that generally very little was known about the aetiology and control of rabbit disease, and he was very well aware of the lack of firm fact in the paper; but he hoped that it would serve as a basis for an interesting discussion from which all could benefit.

### The Opener

**Mr. S. T. Harriss** said that when he was invited to open the discussion on the subject of broiler rabbit diseases, he felt it a great honour to be so asked, but he accepted with some doubt. He felt that everybody he had spoken to was of the opinion that no one knew anything about rabbit diseases, but now the paper had been presented, there was no doubt that Mr. Ostler was a considerable authority on this subject. That left Mr. Harriss wondering where he came in. Was he chosen as a foil?

What he wanted to do was to describe a rabbit breeding plant, similar to that described by Mr. Ostler but which was not connected with broiler production, but which had the same disease problems. It was the set-up with which he was associated for the production of rabbits for research purposes. Here rabbits were not always taken straight out of the nest to be issued for research but usually had to be kept on for some time until they reached certain weights.

Weaning normally took place at 6 weeks, but for certain investigations weaning took place at 4 weeks to allow the doe to be served again. Records had been kept of the rabbits over a large number of years—12 to 15 years—but he did not intend to go further back than 1952. In those days 2 groups of rabbits were kept. The first group was called "paddock" rabbits, and were maintained outside all the year round. The does produced their young in Morant hutches. Rabbits taken out for stock purposes went into modified poultry folds. There were disadvantages in that system. In 1947, for instance, rabbits were not seen for 3 weeks, being buried under snow most of the time. Again, the attendants did not appreciate the outdoor methods under certain conditions and it was difficult to replace them when they left. His chief criticism of the method described was that a walk of up to 2 miles, which was often the distance to be covered by the attendant, was a long distance to carry a dead rabbit, and the records were liable to suffer as a result. Any rabbits over 6 weeks were tattooed in the ear and were entered in the records. Thus it was necessary to justify their existence, but anything under 6 weeks frequently just disappeared.

At the same time a second system of rabbit keeping existed in which rabbits were kept indoors. The does reared their young in tiered hutches and the young were weaned off into colonies. However, male rabbits kept in such colonies fought and castrated each other in fighting, so in order to keep them away from each other, batteries of individual hutches were built and found to be satisfactory. Each one had a water and food hopper.

In 1956 the outdoor system was scrapped and in 1960 another system had since been adopted. The breeding boxes had been retained, but are housed in a better building designed for the purpose. (Mr. Harriss showed a series of slides illustrating the housing.) The system introduced in 1960 mechanised the rearing facilities completely. The new rabbit battery held 1,008 separate cages which were 4 tiers high, and the food and water circulated continuously at intervals of a few minutes. It had fewer disadvantages than the other systems, but had a big advantage over the others in that one man could look after 1,008 rabbits in an hour. It was found that 200 breeding does under the present system provided 4,000 to 5,000 rabbits per annum which were recorded and marked. An important point from the disease angle was that most would doubtless agree that hygiene was beyond reproach. Water and bedding were changed frequently, and food was as fresh as could be obtained. Pellets had even been made by his organisation in order to make sure that what was intended to go into the food did in fact go into it. Careful records of all losses had been kept since 1957.

(Mr. Harriss showed a side illustrating stock rabbit losses from April, 1952, to March, 1958.) Previous to 1957 losses under 4 weeks were not recorded and a mortality as high as 20 per cent. was the maximum. However, when since 1957 all losses were recorded a figure as high as 33.4 per cent. was obtained.

The chief losses were due to intestinal disorders. Coccidiosis took second place, pneumonia third place, accidents fourth place and torticollis fifth place. It was pointed out that nephritis so prevalent in Mr. Ostler's cases did not appear at all as a cause of losses.

Under the age of 4 weeks, losses due to these conditions were almost negligible. Out of 173 such losses, only 10 were due to intestinal disorders, but inanition and stillbirths took their greatest toll. Experiments showed that losses occurred regardless of diet.

In describing a dietary experiment based on 4 different commercial diets, the average conversion rate during the 4 weeks to 12 weeks period with one diet was as low as 4.6, and with others it was 7; but in many individual rabbits it was as high as 14.

Mr. Ostler mentioned that when he changed some diets, deaths in certain instances stopped. It would be interesting to know whether he was getting involved in the current disease of groundnut poisoning. He also mentioned a yeast-like fungus, *Sacchoromycopsis guttulatus*, which had been involved in many rabbit conditions. Whether it was pathogenic or not had not been proved.

With regard to the next killer, coccidiosis, it was found on *post-mortem* examination that there were some 10 intestinal cases to 1 case of hepatic disease. Five days on sulphadimidine reduced infection, but all rabbits again excreted 10 days later. When coccidiosis was so prevalent he wondered whether the frequent diagnosis based on this disease could, in fact, be attributed to *Coccidia* unless really

gross evidence of its presence was evident. He had not found that pneumonia occurred in outbreaks as Mr. Ostler had mentioned, but tended to be more sporadic. A dirty nose was rarely seen.

Rabbits put into individual cages where the weights of diets were recorded very often refused to eat pellets, and a verdict of pneumonia was recorded at *post-mortem* examination when the true cause of death was inanition. In a batch of 32 he found 3 (or about 10 per cent. of the total) which refused to eat pellets. That fact was important and might be worth noting by those who were rearing rabbits for profit.

As to torticollis, he had not found it to be associated with nephritis. He would very much like to know what caused torticollis so frequently. He did not see sore hocks since the wire floors of the cages had been smoothed down with abrasive paper to remove sharp spicules of spelter left behind in the galvanising process.

### The General Discussion

**Mr. O. Swarbrick** (Arundel) said that the rabbit disease which had given him most clinical trouble was the so-called "typhilitis" which occurred in freshly weaned rabbits. The differential diagnosis of that condition was difficult in most cases. The cases which died quite suddenly with an enlarged flaccid colon full of fluid contents were relatively easy. Less simple were those with extensive haemorrhages on the bowel wall, and in which large numbers of coccidia oocysts could be seen in smears of the bowel contents. However, careful inspection of the alimentary mucous membrane and liver often revealed no evidence of inflammatory or ulcerative changes, and one was obliged, often unwillingly, in view of the considerable number of oocysts present, to abandon the attractive and simple diagnosis of coccidiosis. The extreme fragility of the wall of the large intestine in the rabbit rendered examination of the organ difficult. While large numbers of oocysts might be present it was obvious from even a cursory microscopic glance that several species were nearly always involved. He was always amazed that oocysts could be present in the rabbit in numbers so large as to be clinically diagnostic and other species, without any macroscopic lesions. On the one occasion when he considered he observed acute rabbit coccidiosis it was associated with severe enteritis of the colon and caecum with fibrinous peritonitis, loss of weight for a week and severe scouring, although various workers were quoted in the paper to the effect that scouring was not a feature of rabbit coccidiosis. In that case such vast numbers of oocysts of almost exclusively one type were present as to leave little doubt of the diagnosis. Those animals were destroyed, and he had no chance to attempt treatment of the coccidiosis. He would not care to differentiate clinically between various enteric syndromes in the rabbit, but certainly some cases were associated with severe tympany of the colon, which he presumed was very painful. The chief difficulty in his experience in the treatment of this syndrome was its sudden onset and the rapidity of death. Almost any antibiotic given parenterally in the early stages seemed to help, but he had a distinct clinical impression that 1 or 1.5 ml of soluble sulphadimidine was the best, and he liked to think that was at least partially on account of anti-coccidial action. Soluble tetracycline could be put in the drinking water of affected litters at about 600 to 700 mg. tetracycline per gallon, but often the most severely affected animals ate and drank very little. He had not used cortisone, but one would probably use corticoids on any other animal as severely ill as the rabbits, especially as there was strong circumstantial evidence for the implication of some sort of stress factor in the aetiology. The short course of the disease, its rapid onset and the small value of each rabbit were such that professional treatment of individuals was more or less out of the question, and it added to the general difficulties of diagnosis, treatment and control when the attending veterinary surgeon did not see all the cases or the full range of the condition.

He had had no success with various methods of control except the addition of tetracycline to the food at the rate of 100 mg. per ton. When his clients suggested that he was much opposed on general principles and the special grounds that the rabbits' digestion required microbial fermentation processes in the large gut. That had not been borne out in practice and the 2 rabbitries which had thus added antibiotics to their feed had had a much reduced incidence of the condition; but it had not been eliminated. Keeping the young on the doe until slaughter might also substantially reduce the incidence, but would also reduce the total fecundity of the doe. Perhaps in his reply Mr. Ostler would care to comment on the comparative pathogenicity of single as opposed to mixed coccidial infections in the rabbit.

With regard to clostridial infection, he felt that many of the carcases which he had examined with congestion of the small intestine, haemorrhages on the large intestine, often excessive fluid in the pericardium and peritoneal cavities and flaccid colons would certainly have been diagnosed as field cases of "pulpy kidney" in lambs and serum given accordingly. He had never done that with rabbits, but would like the author to enlarge on that possibility, especially as *Clostridia* were so widespread in nature.

**Mr. B. A. Langman** (Kent) asked Mr. Ostler for his comments on the method of administration of medicaments to rabbits, with particular reference to pasteurellosis which was being found in a large number of breeding stock.

Secondly, he was finding a great deal of fatty degeneration in the liver in newly parturient does and wondered whether it had any connexion with metabolic disease.

Thirdly, there was a substance called Amprolium which was used as a coccidiostat, but so far as he could ascertain there was nothing basically scientific to show whether it was efficient for use with rabbits.

### The Reply

**Mr. D. C. Ostler**, in reply, said it was impossible to offer suggestions or direction for the treatment of enteric disease other than on broad lines without knowing the cause. If one could arrive at the cause it would be possible to suggest rational treatment, but at the moment it was only possible to try various therapeutical agents. As to suggesting any particular causes, he was rather confused. It was generally accepted that there was no close correlation between the number of coccidial oocysts in the faeces and the level of infection. He could only suggest that a rabbit should be killed and examined with a view to ascertaining whether there was heavy infestation and whether group treatment was required.

The tetracyclines were of value in some outbreaks of enteric disease. There appeared to be a normal fluctuation in the disease incidence. He had been about to start a trial at a rabbitry where there was a high mortality rate, some 10 or 20 rabbits were being lost a day. It was necessary to delay the administration of the medicated food and the losses stopped shortly afterwards.

Mr. Langman asked for information concerning the control of pasteurellosis. As with rabbit diseases generally, one was not sure of the cause. He could only suggest that precautions were taken to ensure that ventilation and husbandry were satisfactory, and that medication was carried out in accordance with the suggestions made in the paper. The incidence of metabolic diseases in does was not known.

As to Amprolium, he had been informed that there was no information regarding its effectiveness in controlling coccidiosis in rabbits.

**Mr. W. W. C. Gibson** (Ipswich) said he had been trying to find out whether there was a name for the young rabbit.

**Mr. Ostler** replied that there was no special name as far as he knew.

In reply to Mr. Harriss, he was very interested in Mr. Harriss's observations concerning the large number of rabbits which died under the age of 4 weeks. Few rabbits up to 4 weeks of age had been examined as owners generally felt that a small rabbit was not worth bothering about.

The fact that no nephritis was observed in the colony

*(Concluded at foot of p. 1255)*

# The Use and Misuse of Mineral Supplements

BY

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*SUMMARY.—An indication is given of some of the metabolic inter-relationships and antagonisms of minerals commonly used in this country as supplements and additives to foodstuffs for cattle, sheep and pigs; the effects of the deficiency and toxicity of selenium are also briefly discussed.*

*Particular mention is made of some of the harmful effects which may occur when amounts of some minerals, especially copper and calcium, are given in excess of the animal's requirements. It is pointed out that a balance or imbalance of inorganic elements can have a profound effect on the health of the animal, and that therefore mineral mixtures should not be used indiscriminately. When a deficiency is suspected, confirmation should be obtained before mineral supplementation is advised and when possible, parenteral administration of the deficient element under veterinary supervision is the best and safest method of use.*

PERHAPS it would be best to try to outline the scope of this discussion at the outset. It is not my intention to attempt to define the major and minor mineral requirements of farm animals. In my opinion such a definition is still not possible because of the general lack of agreement on, or knowledge of what constitutes minimal requirements for different classes of stock during physiological phases of growth, reproduction and lactation and under varying conditions of management. Five years ago Abrams (1957) very ably reviewed the difficulties and complexities of this subject at a B.V.A. Conference. He pointed out that the metabolism of 1956 was not that of 1900 since the economic rate of weight gain, milk production and level of fertility has changed so much in the last half-century. Economic values have continued to change rapidly in the last five years and now the ever increasing intensification of production imposes new metabolic and nutritional requirements which offer a challenge to those concerned with these aspects of animal health.

Nor is it my intention to discuss the rôle of certain mineral elements in enzyme systems. Just two years ago Owen (1959) gave an interesting and comprehensive review of the connexion between some animal diseases and enzyme systems of which the trace elements cobalt, molybdenum, zinc and perhaps selenium form essential parts.

It is my object to attempt a brief discussion of some of the more practical aspects of inter-relationships and actions of minerals in common use in this country and offered as mixtures for voluntary consumption, for mixing with feeding-stuffs, or for incorporation into proprietary meals and nuts. I will also mention reported effects of the use of selenium, the latest addition to the group of trace elements which play such an important rôle in animal nutrition.

* Paper presented to the Annual Congress of the British Veterinary Association in Oxford on Wednesday, September 6th, 1961.

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**The Diseases of Broiler Rabbits.**—*Concluded.*

might be due to the fact that it was a closed colony, and if nephritis was indicative of infectious disease, one could presume that infection had never been introduced.

As to whether gastro-enteritis was due to groundnut poisoning, he was processing material at the present time to see whether there was any evidence of a toxic food factor. The outbreaks of enteric disease which he had described were unlikely, in his opinion, to be attributable to a simple factor.

Again as snuffles was not a problem in the colony, perhaps it was a specific disease and infection had never been introduced.

Mr. Harriss had made an important observation concerning the dislike which some rabbits had for pellets. Mr. Ostler recalled a number of rabbits which he had examined and which were suffering from pneumonia where the stomachs were completely empty. He did not intend to suggest that torticollis was only related to nephritis. It occurred with middle ear disease which in some cases appeared to occur as a result of secondary infection following parasitic otitis externa.

**Dr. W. R. Wooldridge,** in proposing a vote of thanks, said he did not think that he had enjoyed greater pleasure in the Congress—and he had enjoyed most of the papers he had heard—than he had experienced when listening to Mr. Ostler's paper. One reason was that Mr. Ostler, a young member of the profession, was not afraid to embark upon a developing animal industry, and to try and specialise in it. Further, he had not gone about it in a way which others had so often done in the past, that is, just to record one or two clinical incidents and draw sweeping conclusions from rather brief experience. Mr. Ostler set about making a close survey of the problem in general, and he had recorded his results and set them out in the tables in a most informative way.

In the Animal Health Trust they had learnt the value of those surveys. It had been found almost impossible to make a real attack on any problem of animals which had not previously been closely examined without carrying out a survey, and he felt sure that the author was right in tackling the problem in the way that he had. Furthermore, he was doing that which Dr. Wooldridge had regarded as essential for many years in the profession, namely to gain an intimate knowledge of the animal industry he was studying. Mr. Ostler realised that he must not tackle the problem solely from the angle of pathogenicity. He studied and strove to understand the management problems associated with this new intensive industry. He had been studying how the animals were being kept, and he had applied that knowledge to assist his understanding of the problems of ill health when they arose.

It was with great pleasure, therefore, that he proposed a hearty vote of thanks to Mr. Ostler for his most interesting paper.

The vote of thanks was carried by acclamation.

It is now eleven years since a conference was held in London on "Mineral mixtures in compound feeding-stuffs" at which some of the advantages and disadvantages of the "blunderbuss" or "shot-gun" mineral mixtures were discussed.

During the intervening years we have learned a little of the inter-relations and antagonisms of some mineral elements with others, and their inter-actions with other components of the diet.

Before we knew of these inter-relationships it was thought that if mineral supplements were added to the diet in amounts calculated to make good any deficiency, but small enough to be well below the known toxic level, they could cause no harmful effects, and would merely act as an insurance against any possible deficiency. Our knowledge of the metabolic interactions of this group of nutrients is still pitifully inadequate but there is enough evidence to indicate that some of our beliefs are no longer justified and that we should reconsider some of our ideas on the use of compound mineral mixtures in the light of these relationships.

The problem is made more complex because it is not always a straightforward matter to decide whether a certain disease may be due to "nutritional" or "metabolic" factors, *i.e.*, whether it is caused by a deficiency, an imbalance or an excess of some dietary constituent, or whether it is due to faulty operation of the body's physiological mechanisms for utilising available substances in the body or in the food. Also, it is often difficult to assess the importance to animal health of the total amount of certain mineral constituents in food. Thus, symptoms which are caused by a genuine deficiency of a particular element, can also occur on diets containing apparent abundance of the element, because of the presence of some constituent which interferes with its utilisation by the animal. This type of deficiency is often referred to as a "conditioned" or "induced" deficiency. Conversely, a ration may contain an apparently normal amount of a particular element and yet permit an excessive accumulation of the element in the tissues, leading to toxicity and death. All these complex relationships and antagonisms have to be considered, especially when studying the cause and prevention of mineral deficiency diseases, or disorders of mineral metabolism.

There is a tendency now to think that a compound mineral mixture should be offered *ad lib.* to stock to serve as an insurance policy. Many of these mixtures for ruminants contain calcium, phosphorus, sodium chloride, magnesium and the trace elements iron, manganese, copper, cobalt, iodine and zinc. I shall not discuss to any extent the physiological functions of these elements but will try to relate them to disorders known to occur in some farm animals, excluding poultry.

### Calcium and Phosphorus

Although more experimental work has probably been carried out on the requirements of Ca and P for animals than of any other minerals, it is still not possible to define these with any degree of exactitude. The valuable critical review of Duncan (1958) on studies of Ca and P balance in ruminants makes it abundantly clear that it cannot be assumed that results obtained from balance experiments give "a valid quantitative account of metabolism." She has pointed out that since interpretation of radio-active isotope metabolism studies depend to some extent on the results of conventional balance trials, and are therefore subject to the same errors, it is increasingly important that the limitations of balance experiments should be realised. But much useful information can be obtained from metabolism studies when errors of magnitude are taken into consideration. A critical assessment of published data led her to conclude that "retention of Ca and P depends more on the stage of the life cycle and on the state of the animal's reserves, than on intake, within wide limits. In particular, amounts of calcium provided for dairy cows are often far in excess of their needs and no benefit is obtained from such excess."

The availability of calcium and phosphorus in foods and from various inorganic sources has recently been reviewed (Underwood, 1959; Hill, 1961). The availability of phytate phosphorus which is present in grains in fairly large amounts, is relatively low in pigs and poultry, and phytate may reduce the availability of calcium and other cations in monogastric animals (Hill, 1961). It has been shown, however, that for sheep the availabilities of calcium and phosphorus in calcium phytate are similar to those supplied by monocalcium phosphate (Tillman & Brethour, 1958) and that phytin P of cereal bran is completely digested in the gastro-intestinal system of sheep and cows (Otâ, 1960).

Hill (1961) considers that the evidence regarding availability and absorption indicates (a) that in general the availability of phosphorus for ruminants is appreciably greater than that for calcium which has a moderate rather than a high or very low availability. This applies to all the common sources of the two elements but availability of phosphorus is practically nil from Fe-Al-phosphate and from meta or pyrophosphates, as is calcium from calcium oxalate. (b) Absorption of calcium and phosphorus depends on certain other constituents of the diet such as vitamin D and certain amino-acids and on the requirements of the animal; even a large excess of calcium over phosphorus which would be expected to reduce the absorption of phosphorus, apparently had little effect, although it did depress growth in cattle. The depressing effects of a high Ca : P ratio on growth rate in both adult and young heifers was confirmed in large scale controlled experiments carried out at Weybridge in two successive years (Littlejohn & Lewis, 1960). A reduction in weight gain and feed economy was also found in growing and fattening pigs fed a ration providing a high calcium intake and a wide Ca : P ratio (Bohstedt, 1959). An unexpected, and at present unexplained, mild hyocalcaemia in heifers used in the Weybridge experiment was observed in the two groups receiving a high phosphorus intake; this occurred even in the group receiving supplementary calcium as well as phosphorus in which the Ca : P ratio was 2 : 1 whereas in the other group the Ca : P ratio was 1 : 1. In this experiment, the phosphorus

content of the basic diet (which provided about 8.5 g. P per day) was not high enough to maintain blood inorganic phosphorus levels within the normal range but supplementary calcium providing a Ca : P ratio of about 12 : 1, did not produce a greater decrease in blood inorganic phosphorus levels. This is in agreement with Hill's evidence from a review of the literature (*loc. cit.*).

Following the early work of Theiler, Green and du Toit (1927) it is well known that in growing animals on a phosphorus deficient diet, a fall in blood inorganic phosphorus precedes any outward clinical sign and unless of some duration, does not appear to affect the animal seriously. Continued deficiency in dietary phosphorus leads to reduced fertility in cows (Theiler & Green, 1931-32) and subsequent evidence has confirmed that an intake of phosphorus sufficiently low to produce clinical evidence of deficiency, reduces fertility. But in the absence of such clinical evidence and even when blood inorganic phosphorus values are within the accepted normal range, Hignett and Hignett (1951, 1952) suggested that for high fertility in dairy cattle, the $P_2O_5$ intake should be considerably higher than the generally accepted recommendation (Rations for Livestock, 1957) and that a calcium-phosphorus imbalance caused by both excess of calcium over phosphorus and excess phosphorus over calcium is often associated with a breeding problem. In an attempt to confirm these observations Littlejohn and Lewis (*loc. cit.*) used a basal diet similar to that used by Hignett and Hignett (1952) but which provided a slightly lower phosphorus intake and which resu'ted in a mild degree of hypophosphataemia. Their results failed to demonstrate any significant relationship between the Ca : P ratio of the diet and fertility in dairy heifers, whether the level of herd fertility was high or low. An evaluation of these two somewhat conflicting reports led Hill (*loc. cit.*) to conclude that "the proposed adverse effects of suboptimal phosphorus intakes on fertility in dairy cows that show no clinical evidence of phosphorus deficiency, must be regarded at present as of doubtful validity."

Not only is no benefit derived from the excesses of calcium frequently provided for dairy cows (Duncan, *loc. cit.*) but there is a growing volume of evidence that excessive dietary calcium can, under some circumstances, limit absorption or affect the utilisation of other elements and thus produce a harmful effect on the animal.

The depressing effect on growth has already been mentioned. Recent reports suggest a reciprocal relationship with magnesium. The existence of a common transport system for absorption of calcium and magnesium has been postulated (MacIntyre, 1960). Support of this hypothesis is given by the findings of: (1) Alcock and MacIntyre (1960) who found increased calcium absorption in rats on a magnesium-deficient diet and increased magnesium absorption in rats fed a calcium-deficient diet, (2) Allcroft, Lewis and Burns (1961) who showed that addition of calcium lactate to the diet of calves fed exclusively on milk, caused the expected hypomagnesaemia to occur earlier and become more severe. It would therefore seem possible that the hypomagnesaemia of the milk-fed calf may be attributable in part, at least, to an abnormally high intake of calcium and could therefore be regarded as a conditioned deficiency of magnesium.

This effect of excess dietary calcium on absorption of magnesium and on growth rate make it pertinent to consider that many modern rations for cattle and sheep supply very high intakes of calcium. For example the majority of proprietary pelleted rations for cows, calves and sheep contain from 1 to 4 per cent. of a mineral supplement consisting of limestone, bone flour and salt. These concentrate rations are frequently fed as well as grass, hay and silage. Legume hays, and to some extent, grass-clover hays are very high in calcium. In addition most stock are offered *ad lib.* compound mineral mixtures which may contain a high percentage of calcium as limestone, bone flour or dicalcium phosphate and often contain limestone as well as either of the other calcium-phosphorus compounds. Thus, the heavily yielding dairy cow, or the calf which is being "done extra well," may be ingesting excessive amounts of calcium in relation to magnesium and other essential minerals, thereby causing conditioned deficiencies.

Other limiting effects of excess dietary calcium have been reported. For many years now there have been indications that ingestion of excessive calcium can increase goitrogenic effects. Simpson (1947) found that in rats on a low iodine diet, an increase in iodine excretion and a fall in iodine content of the thyroid occurred when the calcium content of the diet was increased. More recently Taylor (1954) reported evidence which indicated that too much calcium was a contributory cause of goitre.

The inter-relationship of zinc and calcium in the development of parakeratosis in pigs is well known. This disease occurred widely in the U.S.A. in pigs fed dry rations composed chiefly of corn, vegetable proteins, vitamins and minerals. During 1956 - 57 it was shown (Lewis, Hoekstra, Grummer & Phillips, 1956; Stevenson & Earle, 1956; Luecke, Hoefer, Brammell & Schmidt, 1957) that zinc deficiency in pigs could be aggravated and growth rate decreased by high dietary levels of calcium. In these studies symptoms occurred when as much as 30 to 35 p.p.m. Zn were present in the diet even with normal calcium levels of 0.48 to 0.82 per cent. Higher levels of calcium caused increased signs of zinc deficiency and when levels of 1.03 to 1.42 per cent. calcium as limestone was used, 80 to 100 p.p.m. Zn was required to prevent symptoms. Lewis *et al.* (1956) found that similar effects were obtained whether the additional calcium was supplied as bone meal, limestone or dicalcium phosphate.

Parakeratosis has not been as widespread in Britain as in the U.S.A. This may be due to the use of more animal protein in pig rations here and to the wider use of wet feeding than in the U.S.A. Even though other dietary factors as well as calcium may be concerned in development of the syndrome there seems little doubt that it is associated with addition of supplementary calcium which causes a conditioned deficiency of zinc.

**Magnesium**

In view of the recent B.V.A. Conference on hypo-

magnesaemia, the only aspect I shall mention here is that relating to the use of oral magnesium supplements for prevention and control of the disorder.

At the outset it should be stated that the feeding of magnesium supplements to animals whose magnesium status is normal, will not provide a depot of readily available magnesium for emergency use; therefore, the provision of such supplements to normal animals during non-susceptible periods is useless as a prophylactic measure. This point does not seem to be sufficiently appreciated and it is remarkable how often the directions for use accompanying magnesium-rich mineral supplements or pelleted feeds, do not mention this aspect. Even when directions are supplied the wording may be so vague that the farmer could not be blamed for thinking the use of these supplements several months or weeks before a period of hypomagnesaemia might be expected to occur, would afford subsequent protection to his cattle or sheep.

It has been suggested (Blaxter & McGill, 1956) that the bones, or bone crystal surfaces, provide a labile reserve of magnesium which can be drawn on in the absence of a dietary source or when there are increased demands from tissues as in rapid growth, augmented lactation, or increased secretion of magnesium into the digestive tract. Cunningham (1936) found no difference in the magnesium content of bones from normal adult cattle and from cows affected with hypomagnesaemic tetany. Similar results obtained at Weybridge indicate that the magnesium in the bone of adult cattle does not provide a readily mobilisable reserve.

MacIntyre and Davidsson (1958) showed that there was little or no change in the total magnesium content in the femur, although the femur magnesium concentration declined in the growing magnesium-deficient rat. MacIntyre (1960) suggested that the concept of the skeleton as a magnesium reservoir should be discarded, and that it should be recognised that magnesium deficiency, whether occurring in man or in the experimental animal, involves the body cells. Evidence in favour of this was provided by: (1) MacIntyre and Davidsson (*loc. cit.*) who found there was a decline in magnesium concentration in skeletal muscle of rats after 64 days on a magnesium-deficient diet. This finding is in contradiction of some earlier reports (Watchorn & McCance, 1937; Blaxter, 1956; Parr, 1957); (2) Allcroft, Lewis and Burns (1961) who found a progressive fall in the skeletal muscle magnesium of hypomagnesaemic calves, the decrease being proportional to the duration of the hypomagnesaemia.

Blaxter (1954) attributed the hypomagnesaemia of the milk-fed calf to a simple dietary deficiency. Smith (1957) considered that a milk diet provided more than adequate magnesium for calves up to about 5 weeks of age, and that the hypomagnesaemia which sooner or later appeared as the calves got older, was associated with a progressive decrease in their ability to utilise dietary magnesium. He suggested that this could be caused by a decrease in absorption or an increase in endogenous faecal excretion, or a combination of these; or, alternatively, the changes involved may be caused, at least in part, by an abnormal condition arising from the particular properties of the milk diet, among which a high calcium content must be considered.

It is a debatable point whether all types of hypomagnesaemia can be attributed to a dietary deficiency of Mg particularly that occurring in cows grazing rapidly-growing spring pasture when the serum Mg level can fall sharply within a few days. Available evidence indicates that there are factors other than the actual amount of Mg present in the diet. Dutch workers (Brouwer, 1952; Kemp & 't Hart, 1957) have for some time related occurrence of hypomagnesaemia to an imbalance of inorganic constituents in pastures associated with excessive use of potassium and nitrogen fertilisers; this in time appears to reduce the "availability" of herbage magnesium (Kemp, Deijs, Hemkes & van Es, 1961).

The presence of factors affecting the availability of magnesium in quickly growing grass and other foodstuffs may well account for the relatively large quantities of Mg supplements necessary for prevention of hypomagnesaemia in cattle and sheep. Thus the minimum prophylactic dose for adult cattle grazing a tetany-prone pasture is approximately 56 g. (2 oz.) of magnesium oxide or calcined magnesite given daily during the susceptible period, in addition to the magnesium already supplied by the food (Allcroft, 1954; Line, Head, Rook, Foot & Rowland, 1958). The amount required for prophylaxis in calves depends on the age of the animal and the available dietary Mg, but in general $\frac{1}{4}$ to $\frac{1}{2}$ oz. of magnesium oxide or twice this amount of magnesium carbonate should be given daily. For restoration of a normal magnesium status in a hypomagnesaemic calf, requirements depend on the duration and degree of the hypomagnesaemia as well as the age of the calf, but results obtained by Parr (1957) suggest that the daily supplement should not be less than $\frac{1}{2}$ oz. magnesium oxide for this purpose. Little information is available on minimum prophylactic doses for sheep but it would seem to be in the region of $\frac{1}{3}$ oz. daily. It is difficult to control intake of supplementary Mg in grazing ewes irrespective of whether it is offered as calcined magnesite alone, in mineral mixtures, mixed with cereal concentrates or incorporated in pelleted feeds; invariably some ewes will consume too much which may cause scouring, and others will eat too little or none at all. This difficulty of ensuring an adequate supplementary intake also applies to beef catttle at grass and especially to suckling calves in which the incidence of hypomagnesaemia is sometimes high. Apart from drenching them at frequent intervals or inducing them to eat supplemented cereal or concentrate feeds, there is little information on effective methods of control in this age group of stock.

Even though the prophylactic dose of magnesium for different classes of stock is well known to the veterinary surgeon, it may not be well known to the farmer who buys what he thinks is a suitable "tetany mixture" but which in fact contains an inadequate amount of magnesium. Watt (1960) has recently drawn attention to this and it would seem that some

action from the veterinary profession might help to remedy this position.

**Iron**

Under naturally occurring conditions, iron deficiency has not been demonstrated in sheep, cattle or horses and its occurrence seems improbable in view of the liberal amounts of iron in most feeds relative to their requirements (Underwood, 1956). Even during the suckling period, iron deficiency is unlikely to occur in these species, but if they are maintained on milk alone for an abnormally long period, a mild anaemia may occur. In an experiment at Weybridge in which 16 calves were muzzled and kept on a milk diet alone for 12 to 16 weeks, haemaglobin values fell below 9 g. per 100 ml. blood in only two animals, the minimum value reaching 7.5 g. per 100 ml. Blaxter, Hutcheson, Sharman and Macdonald (1957) investigated the occurrence of iron-deficiency anaemia in calves of beef cattle in which the rearing system was characterised by a large daily intake of milk and the solid food intake was usually small. Under these conditions only a very mild anaemia was found.

In pigs, however, iron-deficiency anaemia is frequently a problem in the young during the first part of the suckling period, especially in animals reared in concrete pens without access to soil or pasture. The rapidity of the development and the severity of anaemia in piglets compared with the slowly developing mild anaemia which is usual in calves, if indeed any occurs at all, are understandable when the relative growth rates of piglets and calves are compared.

Greig (1960) has recently reported that high supplements of calcium carbonate fed to fattening pigs from weaning onwards, caused an iron deficiency as shown by reduction in haemoglobin levels and rates of live-weight gains. These effects were especially marked in litters with low weaning weights. Injections of iron dextran at weaning overcame these effects. In a further experiment in which no supplementary calcium carbonate was added to the diet of pigs whose haemoglobin levels were already high, injection of iron at weaning did result in increased weight gains over a four week period. On the basis of these results, Greig suggested that if fattening pigs are to realise their full potential, they must have a sufficiency of iron and if the diet is high in calcium carbonate, their requirement for iron is increased.

**Manganese**

Symptoms of manganese deficiency in mice, rats and rabbits kept on milk or synthetic diets very low in manganese have been recognised for the last 30 years. Although similar, the symptoms in these three species are not identical and are characterised by impaired growth, defective mineralisation and structure of the bones, and depressed reproductive function in both males and females (Underwood, 1956).

The importance of manganese in avian nutrition is well known and will not be discussed here. In the larger farm animals, manganese deficiency is likely to be rare, especially under the usual conditions of grazing and stall management and even rations containing a high proportion of skim-milk appear to supply adequate manganese for normal requirements for pigs.

To determine the quantitative requirements of pigs for manganese and to observe the symptoms of manganese deficiency in growing and reproducing boars and gilts, Plumlee, Thrasher, Beeson, Andrews and Parker (1956) fed semi-purified rations containing 0.05 to 40 p.p.m. manganese. Second generation boars from gilts raised on rations containing either 1.0 or 3.4 p.p.m. manganese, grew normally and showed normal spermatogenesis when fed a ration containing 3.3 p.p.m. manganese from a mean initial weight of 43 lb. to a mean final weight of 246 lb. When 20 female pigs were weaned at three weeks of age and at a mean weight of 9.4 lb., divided into two equal groups and fed throughout the growing, gestation and lactation period on a ration containing either 0.5 or 40 p.p.m. manganese, those fed the higher manganese diet shrowed no abnormalities but those on the lower manganese diet developed deficiency symptoms which began to appear at an average weight of about 55 to 60 lb. All showed reduced body length and height and shorter legs but only half exhibited bowed legs or enlarged joints. Other symptoms included increased fatness, irregular or complete absence of oestrus, resorption of foetuses or birth of small weak piglets which showed incoordination and lack of balance, poor udder development and agalactiae. Analysis of tissues showed 10 to 20 per cent. lower manganese levels than those of the control gilts fed the higher manganese diet. The authors concluded that since average pig rations contain over 20 p.p.m. manganese, it is most unlikely that such a deficiency would occur under natural conditions unless caused by some interfering dietary substance.

There have been suggestions from this and other countries that a simple or a "conditioned" deficiency of manganese can effect the health and fertility of cattle but little reliable information exists apart from the report of Bentley and Phillips (1951). These workers fed a group of young Holstein heifers from calfhood through one, two or three lactations on rations containing 7 to 10 p.p.m. manganese, and other groups on the same basal rations supplemented with manganese sulphate to bring the manganese content to 30, 40 and 60 p.p.m. Mn respectively. It was concluded that concentrations of 10 p.p.m. Mn are adequate for growth but might be marginal or borderline for optimum reproductive performance since there was some delay in onset of oestrus and a slightly reduced conception rate in the group on the low manganese rations. In this basal group there was also a greater number of calves born at the first calving with weak legs and pasterns. There was no difference in the total and inorganic phosphorus blood values of heifers on the basal diet or on the diet containing 60 p.p.m. Mn, but no analysis for inorganic or organic constituents of bone were made nor was the copper status of these animals reported. Comparison of manganese contents of various tissues from the animals, showed that the low manganese diet did not reduce the manganese content of any organ except the ovary, in which a reduction of 50 per cent. or more was found giving a mean value of 0.8 p.p.m. dry weight compared with

2.0 p.p.m. for ovaries from animals on rations containing 30 p.p.m. manganese.

In another experiment Bentley, Quicke, Kastelic and Phillips (1951) studied the distribution of manganese and cobalt in foodstuffs and tissues of cows with low fertility in Wisconsin. The manganese content of the hay fed to these cows ranged from 8.9 to 48.5 p.p.m. and in some instances the cobalt content was low or marginal. Manganese values for the ovaries from 8 of these cows ranged from 1.5 to 3.1 p.p.m. which were only slightly lower than values (2 to 3 p.p.m.) from animals fed adequate manganese. It was concluded that no single cause was responsible for the infertility and that trace minerals had little if any direct relationship to the problem.

Russell and Duncan (1956) reported a manganese deficiency syndrome occurring in cattle in the Netherlands and described by Grashuis, Lehr, Beuvery and Beuvery-Asman (1953). The heifers were poorly developed, had straight hocks and upright pasterns sometimes with knuckling over of the fetlocks and had a low fertility. The manganese content of the ovaries of a yearling heifer was 0.6 p.p.m. compared with a value of 2.2 p.p.m. for a normal 2-year-old heifer; the liver copper content of both animals was low, 6.0 and 8.8 p.p.m. respectively. The manganese content of pastures from affected farms was below 100 p.p.m. in 57 per cent. of the samples; 150 to 250 p.p.m. were regarded as sufficeint; the soil *p*H was high. Grashuis has claimed good results from administration of manganese to similarly affected heifers on farms where the soil *p*H was high.

There is a considerable variation in the manganese content of pastures from different areas as well as seasonal and species differences. Many values from different countries have been reported as lying between 20 and 100 p.p.m. (Russell & Duncan, *loc. cit.*). Seekles (1960) reported that analysis of 645 samples of pasture and hay from different parts of the Netherlands gave average pasture values of 191, 152, and 114 p.p.m., and hay values of 181, 167 and 95 p.p.m. from sandy, peat and clay soils respectively. He also reported a wide variation in the manganese content of ovaries from cattle but no significant differences were found for different age groups. In his view, no conclusive evidence has so far been obtained of a relation between manganese and decreased fertility in cattle in the Netherlands.

Hignett (1941) suggested that manganese deficiency leads to ovarian dysfunction in cattle and later (1956, 1959) produced evidence to support the view that the dietary level of manganese necessary for high female fertility depends on the relative amount of certain major minerals and perhaps other nutritional factors. In experimental studies of the relationship between the calcium-phosphorus ratio of the diet and fertility in heifers, Littlejohn and Lewis (*loc. cit.*) also examined the relationship of manganese to the calcium and phosphorus contents of the diets. In those groups in which an adequate comparison was possible with results reported by Hignett (*loc. cit.*). there was no evidence in support of his observations.

Russell and Duncan (*loc. cit.*) pointed out that Bentley and Phillips (*loc. cit.*)were not able to produce deficiency symptoms in dairy cattle when the diet contained as little as 20 p.p.m. Mn, and that there are several discrepancies between their findings and the syndrome reported by Grashuis *et al.* (*loc. cit.*). The latter authors considered that unusually high Ca, P, Fe and protein contents of the pastures raised the requirement of the cattle for manganese. Grashuis (personal communication) has stated that his reports of the syndrome and response obtained to administration of manganese are field observations and the syndrome has not been reproduced experimentally.

It is obvious that more experimental work is necessary to clear up the existing discrepancies and in the meantime, field reports of abnormalities related to manganese deficiencies or excesses in the diet should be examined critically and cautiously.

**Copper and Molybdenum**

Because of the inter-relationship of these two elements in ruminant metabolism, it is necessary to discuss them together. The occurrence of copper deficiency in cattle and sheep in this and other countries, and copper toxicity in sheep in parts of Australia on pastures of apparently normal copper content, is now well established. It is therefore obvious that there are dietary factors which influence absorption and retention of copper in these two species other than the actual amount of copper ingested. The two factors which have been studied most intensively are the molybdenum and sulphate contents of the rations in relation to the copper content. Russell (1944) suggested the reciprocal antagonism between molybdenum and copper when reviewing the work of Ferguson, Lewis and Watson (1943) which showed that "teart," a scouring disease of cattle caused by high intakes of molybdenum, responded to copper therapy. This relationship was confirmed by Dick and Bull (1945) in Australia, by Cunningham (1950) in New Zealand and by Allcroft and Lewis (1956a) in Britain; the mechanism of the reaction is not yet understood.

During 1953-56 Dick (1956) showed that the inorganic sulphate content of the diet of stalled sheep, influenced the effect of molybdenum on copper metabolism. He demonstrated that when the sulphate intake is high (2 to 10 g. per day), (a) molybdenum retention is limited by a reduction of intestinal absorption and an increase in excretion, (b) the effect on blood and tissue copper in the sheep is related to the molybdenum intake so that (i) at very high molybdenum intakes (say 80 mg. per day) there will be an immediate rise in blood copper; tissue copper will remain unchanged but physical signs of copper deficiency may appear, *e.g.* fleece lesions; (ii) at lower molybdenum intakes (*e.g.* 20 mg. per day), the rise in blood copper occurs after a period of delay depending on the molybdenum and sulphate intakes: (iii) tissue copper falls at a rate also dependent on the molybdenum and sulphate intakes. When tissue copper is sufficiently depleted, there will be a sharp fall in blood copper and clinical copper deficiency symptoms will occur. A high molybdenum intake alone or high sulphate intake alone is without effect on either blood or tissue copper under these dietary conditions.

Dick suggested that some of the discrepancies in results reported from Australia and Britain, such as the occurrence of swayback and of copper deficiency in cattle on pastures of apprently normal copper and molybdenum contents, might be caused by the different intakes of inorganic sulphate under the conditions for which the observations were recorded. However, analysis of pasture samples showed that occurrence of copper deficiency in cattle and sheep in Britain could not be explained in terms of their copper, molybdenum and sulphate contents (Allcroft & Lewis, 1956b). Cunningham (1955a) also reached the same conclusion regarding the pasture-animal relationship in New Zealand. He (1955b) reported that under New Zealand conditions, the pathological effect of molybdenum on cattle is determined by the relative amounts of copper and molybdenum in the pastures. A moderate excess of molybdenum causes the disorder only if the pasture copper is below normal. For example, if the pasture contains about 10 p.p.m. copper then about 20 p.p.m. molybdenum must be present before toxic effects are produced; for lower levels of copper the minimum harmful level of molybdenum is lower, so that molybdenum is harmful at levels of 3 to 7 p.p.m. when pasture contains only 3 to 5 p.p.m. copper. This relationship does not always hold in Britain; on pastures with mean copper and molybdenum values of 24 and 7 p.p.m. respectively, associated with a wide range of sulphate values, severe copper deficiency in cattle has been found.

During the last 10 years experimental observations have been made on sheep on the effect of feeding different diets with varying copper, molybdenum and sulphate contents, some of the diets consisting almost entirely of greenstuffs and others of hay and concentrates. The effects of liver copper storage were inconsistent and conflicting and it was concluded (Lewis & Allcroft, 1960) that in the various diets used, there are factors other than total copper, molybdenum and sulphate concentrations which influence copper absorption and retention in sheep.

It has been observed by Dutch and British workers that the copper status of sheep and cattle frequently improves when the animals are housed and fed rations of hay and concentrates with a lower copper content than spring and summer grass. This suggests that fresh grass contains substances which influence absorption of copper. Deijs and Bosman (1961) who have been investigating the copper-binding activity of components of fresh grass, suggest that the porphyrins might be considered as being one of the factors which may affect the utilisation by cattle of copper in fresh green herbage.

Because of the complexity of copper metabolism in sheep and cattle it should be evident that it is not possible to predict the probable copper status of animals from chemical examination of samples of feeding-stuffs or of soils in this country except perhaps in the case of obviously "teart" pastures. And since adult sheep may have a very low copper status without showing a recognisable clinical abnormality, and since the signs of copper deficiency in cattle are not pathognomonic, a clinical examination is not always a reliable guide. A suspected deficiency should be confirmed by differential diagnosis and by chemical analysis of blood or liver to assess the copper status before any form of therapy is recommended.

It is well known that copper is an essential nutrient with a specific physiological function and that the liver is the chief organ of storage within the body. It is perhaps not so well known that there is a marked species difference in the normal range of copper in the liver, as well as an appreciable individual variation which is common to all species (Underwood, 1956). For example the liver copper concentration of normal adults of most species usually lies between 10-50 p.p.m. on a dry matter basis with a high proportion falling between 15-30 pp.m. (Beck, 1956). These levels are found in species as unrelated and as diverse in their environment and their nutritional habits as man, rats, rabbits, cats, dogs, foxes, pigs, kangaroos, whales, crocodiles, snakes, domestic fowls and turkeys, emus, sharks and herring (Underwood, *loc. cit.*). But a few unrelated species have very much higher liver copper values ranging between 100-400 p.p.m. These include the sheep, cow, duck, frog and several species of fish (Beck, *loc. cit.*). From a consideration of the data, Beck suggested that the high liver copper level characteristic of some species is due, not to a higher intake of copper or to a greater absorption, but to a lesser ability to restrict the storage of copper in the liver and to excrete stored copper. This applies particularly to the sheep which is known to be very susceptible to copper poisoning. On the other hand, some species are extremely tolerant to high doses of copper, *viz.*, the rat and domestic fowl (Cunningham, 1931).

Under some conditions of management, sheep will accumulate copper very readily even on diets supplying apparently normal amounts of copper, molybdenum and sulphate. Our toxicological records at Weybridge have shown an increase in the number of cases of chronic copper poisoning over the last few years. This has been associated with the widespread use of mineral supplements containing copper, with the addition of copper among other minerals, to pelleted feeds for sheep, and even with the use of pelleted feeds with a copper content of about 25 p.p.m. to which no supplementary copper had been added.

Our observations have shown that on some diets, the liver copper concentration of stalled sheep will increase rapidly and substantially even though the total copper concentration of the ration is not abnormally high. For example, stalled sheep which were fed on hay and a concentrate mixture of crushed oats, bran and linseed cake which provided essentially normal intakes of copper, molybdenum and sulphate, of about 12 p.p.m. Cu, 1 p.p.m. Mo and 0.7 per cent. $SO_4$, accumulated abnormally high concentrations of copper in their livers; some died showing symptoms typical of chronic copper poisoning.

Recently there have been outbreaks of copper poisoning in 3- to 10-month-old lambs as well as in older sheep. In some cases the lambs were at grass, in others they were housed; all were fed proprietary nuts or concentrate mixtures. The copper content of

the nuts ranged from about 20 to 80 p.p.m.; it was known that small amounts of copper had been included as copper sulphate in some of the nuts. We have observed that the addition of only small amounts of copper sulphate, to supply as little as 5 mg. Cu per day, will lead to a marked accumulation of copper in sheep on certain diets. It is known too, that young calves reared on milk substitutes to which copper sulphate has been added to bring the copper content to 60-100 p.p.m., may store dangerous amounts of copper (Shand & Lewis, 1957).

The pig, which has a low liver copper level (although its average blood copper level of 140 $\mu$g. per 100 ml. was the highest Beck (*loc. cit.*) found among the species he examined) is very tolerant to high copper intakes. Barber, Braude and Mitchell (1955) and Braude (1957) found that addition of 0.1 per cent. copper sulphate supplying 250 p.p.m. Cu to a fattening pig diet increased growth rate significantly without causing harmful effects under the conditions relating to their trials.

Although there is now much evidence that meals supplemented with copper sulphate at the 0.1 per cent. level have not only caused no untoward effects but have increased rate of growth in fattening pigs, it appears that under some circumstances this level can cause a syndrome similar to chronic copper poisoning (Gordon & Luke, 1957; O'Hara, Newman & Jackson, 1960; Buntain, 1961). Even though these occurrences are few, it should be recognised that excessive concentrations of copper in the tissues of pigs can represent a potential, although in most instances only a slight hazard. Additions of 0.2 and 0.4 per cent. copper sulphate to fattening pig rations have been found to produce toxic effects (Allcroft, Burns & Lewis, 1961) whereas Lucas and Calder (1957) reported that addition of 0.05 per cent. produced a growth-promoting effect without causing excessive storage of copper in the liver similar to the growth-promoting effect obtained by Barber *et al.* (*loc. cit.*) by addition of 0.1 per cent. which can cause excessive liver copper storage.

For most species the concentration of copper in the liver reflects the concentration of copper in the diet except where interfering factors cause a conditioned deficiency as in grazing sheep and cattle in many parts of the world. In some species, however, the copper intake may vary within fairly wide limits without a corresponding change in liver copper concentration (Beck, *loc. cit.*). This is so in the pig. Lucas and Calder (*loc. cit.*) showed that levels of dietary copper from 5 to 60 p.p.m. caused no significant change in liver copper contents of pigs; dietary levels up to 125 p.p.m. caused moderate increases in liver copper content but at 250 p.p.m., liver copper values increased substantially.

The sheep and the cow differ from most other mammalian species, in that, within the normal range of diets, the concentration of copper in their livers varies with the intake (Beck, *loc. cit.*). This is particularly so with regard to the sheep where not only the total dietary copper but also other dietary factors can profoundly influence liver copper storage. It is for this reason that much more discrimination and caution should be exercised concerning the giving of mineral supplements containing copper to sheep.

Copper supplementation to copper deficient ewes is essential for prevention of swayback in the lamb but the indiscriminate use of copperised mineral supplements and their addition to pelleted feeds represents a misuse of minerals which veterinary surgeons should do their best to prevent.

This tendency to rapid and excessive accumulation of copper by sheep and young calves under some dietary conditions is particularly important under present-day trends of intensive methods of management and zero-grazing.

It is usual for most mineral mixtures to contain copper in amounts thought to be sufficient for the type of stock for which they are intended, but not in excessive amounts. The difficulty is in knowing what will be an excessive amount. Under some conditions, only a few extra parts per million could be excessive and could cause toxic effects. It is wrong to suppose that the presence of small supplements of copper can do no harm if copper deficiency does not occur in a particular flock and that the supplements will merely act as an insurance against the possible occurrence of a deficiency. The complexity of copper metabolism in ruminants and the known and unknown factors which must be considered when trying to make a diagnosis of, or recommend prophylactic treatment for copper deficiency are evident. It is my opinion that copper supplements should be given to sheep in this country only during pregnancy for prevention of swayback in their lambs. For this purpose an adequate and safe dose is most easily administered by injection of suitable copper compounds (Allcroft, Clegg & Uvarov, 1959).

Apart from the advantage of allowing the operator to administer the amount of copper thought to be desirable for individual animals depending on age, copper status and severity of the copper-conditioning factors present in the herbage, it has been demonstrated that injected copper is less readily excreted than orally administered copper. Comar (1950) found that about 78 per cent. of orally administered copper was excreted in the first five days after administration to cattle compared with only 6 per cent. of an intravenously injected dose of radioactive copper. It has been shown too, that one dose of 240 mg. Cu as copper glycine injected subcutaneously maintained an adequate copper status for four months in cattle on a farm where a severe copper deficiency developed after a few months grazing (Allcroft & Uvarov, 1959). Previous work had shown that 300 mg. Cu as copper sulphate injected intravenously into cows grazing "teart" pastures controlled scouring for about six weeks whereas 500 mg. of orally administered copper was required at approximately daily intervals to produce the same effect (Allcroft, 1952).

### Selenium

Before the identification (Schwarz & Foltz, 1957; Patterson, Milstrey & Stokstad, 1957) of selenium as an integral constituent of "Factor 3" (a previously unknown agent protecting rats against dietary necrotic liver degeneration) the only veterinary interest in

this element was related to the disorders and losses in stock resulting from consumption of herbage containing toxic amounts of selenium. The most well-known distribution of seleniferous soils and vegetation is in the western half of the U.S.A., but wheat containing 1 to 2 p.p.m. Se has been obtained from many other parts of the world (Trelease, 1945), and small seleniferous areas have been found in Eire (Walsh, Fleming, O'Connor & Sweeney, 1951) and in Australia (Knott, McCray & Hall, 1958).

The naturally occurring disorders are known as "alkali disease" and "blind staggers" and were thought to be manifestations of chronic and acute selenium poisoning respectively (Moxon & Rhian, 1943), but more recent work suggests that both these syndromes come within the category of chronic selenosis. Rosenfeld and Beath (1946) reported that blind staggers in cattle in Wyoming is caused by selenium poisoning. This syndrome is considered to be identical with polioencephalomalacia, a non-infectious disease of cattle and sheep on pasture and feedlot in Colorado and is known as "forage poisoning," the cause of which has not been determined (Jensen, Griner & Adams, 1956). The absence of the clinical signs described as characteristic of chronic selenium poisoning (Moxon & Rhian, *loc. cit.*) in the cattle population in Colorado where polioencephalomalacia is common, is irreconcilable with the theory that this disease is caused by selenium poisoning (Jensen *et al.*, *loc. cit.*) Maag, Orsborn & Clopton (1960) reported that seleniferous plants can produce either acute or chronic poisoning, the toxic effect depending on the type of selenium compound present, the type of experimental animal, the criterion of toxicity and the experimental conditions. To determine the effect of sodium selenite on cattle under typical feedlot conditions, Maag *et al.* (*loc. cit.*) fed a ration of ground grain, alfalfa hay and molasses plus selenium (as sodium selenite) from 0.25 to 0.50 mg. per pound bodyweight over a period of 28 weeks. Few signs typical of alkali disease, blind staggers or forage poisoning developed; cumulative effects were not produced at the lower level of the Se dosage. In earlier studies, the ill effects of feeding seleniferous plants to livestock have been attributed solely to the presence of selenium in the plants. Maag *et al.* (*loc. cit.*) suggest that alkaloids and other toxic substances which have been found in many of the seleniferous plants may cause the syndromes attributed to selenium poisoning in cattle and sheep.

The report of Maag *et al.* (*loc. cit.*) and the well-known fact that the toxicity of selenium is influenced by dietary factors such as the protein content of the diet and other constituents (Moxon & Rhian, *loc. cit.*) suggests that the toxicity of selenium for cattle and sheep should be re-investigated under conditions pertaining to its use under different conditions and in particular areas. This is particularly important now that selenium has been shown to be involved in essential biological functions of many of our domestic animals and in view of the similarity of the lesions in polioencephalomalacia and those in cerebrocortical necrosis in cattle and sheep (Terlecki & Markson, 1961).

Schwarz and Foltz (1958) showed there is a marked difference in the biopotency of selenium compounds. They divided them into three main categories with respect to biopotency against liver necrosis in rats: (a) elementary selenium and certain inorganic and organic compounds are practically inactive; (b) a second group including most inorganic selenium compounds such as selenate and selenite, many organic selenium compounds, and also the selenium analogues of cystine, cystathionine and methionine which have a 50 per cent. effective dose ($ED_{50}$) of about 0.02 to 0.03 p.p.m. Se (2 to 3 $\mu$g. per cent. Se); (c) the third group of higher biopotency is small and so far only four synthetic organic compounds have been found to be more active than selenite but none of them reaches the biopotency of "Factor 3" which has an $ED_{50}$ of about 0.7 $\mu$g. per cent. Se. A daily dose of 0.1 $\mu$g. of Factor 3-Se fully protects rats against death and significantly enhances growth. This requirement is in accordance with amounts of selenium found in natural foods which are of the order of 0.05 to 10 $\mu$g. per g. of dry matter. An estimation of selenium does not give an estimation of "Factor 3" activity since some foods contain the element in a biologically inert form; Factor 3-selenium is the most effective selenium compound thus far known (Schwarz & Foltz, *loc. cit.*)

In a recent review Schwarz (1960) clarified some of the relationships of selenium and vitamin E. He states that so far, there appears to be three groups of diseases which must be separated:

(1) Those caused by vitamin E deficiency which are not influenced by Factor 3-selenium even in large excess; resorption sterility in rats and encephalomalacia in chicks come into this category. (2) Those caused by Factor 3-selenium deficiency which are not affected by vitamin E, such as a disease entity in rats comprising lack of growth, muscular wasting, adrenal atrophy and pancreatic dystrophy, and also a growth effect in the chick. [It appears that a growth effect in the lamb can be added to this list—see following discussion.] (3) Those caused by a simultaneous deficiency of both factors. To this group belong dietary liver necrosis in the rat, liver necrosis and muscular dystrophy in the pig, multiple necrosis in the mouse, heart and peripheral muscular dystrophy in the mink, and exudative diathesis in chicks and turkeys.

Thus, dietary liver necrosis is essentially the result of the simultaneous lack of Factor 3-selenium and vitamin E, and although a lack of either of these factors alone often produce relatively mild chronic diseases, the simultaneous deficiency of both leads invariably to acute tissue damage and to death. Methionine and cystine, when supplied at levels exceeding the requirement for growth, may delay the onset of liver necrosis as a result of a sparing effect on the requirement for vitamin E, but they do not prevent it (Schwarz, *loc. cit.*). The clarification of these relationships may help to explain some of the complexities and anomalies reported in liver necrosis and muscle degeneration syndromes in pigs. Schwarz points out that a number of diseases, hitherto attributed solely to vitamin E, are of dual origin and that the presence or absence of Factor 3-active

selenium determines the fate of an animal on a vitamin E deficient diet.

In the last few years it has been demonstrated that Se plays an important rôle in the prevention of muscular dystrophy and poor thriving conditions in sheep and calves. Muth, Oldfield, Schubert and Remmert (1959) showed that the incidence of white muscle disease in lambs was significantly reduced when their mothers were fed on a ration previously known to produce the condition and to which 0.1 p.p.m. Se (as sodium selenite) was added; addition of vitamin E to the diet was without effect. In a later experiment, Oldfield, Muth and Schubert (1960) reported that addition of 0.1 p.p.m. Se to a ration for ewes from the third month of pregnancy onwards, or intramuscular injection of 1.4 mg. Se to lambs soon after birth (in both instances as sodium selenite) prevented white muscle disease and resulted in increased growth of lambs as compared with untreated controls. The growth response of the lambs was greater when Se was fed pre-natally than when it was injected post-natally. Large doses of vitamin E at birth protected lambs from white muscle disease but did not result in improved growth.

Results of trials in New Zealand (McLean, Thomson & Claxton, 1959; Drake, Grant & Hartley, 1960) confirmed and supplemented the Oregan reports: α-tocopherol was of no value when given to pregnant ewes 1 to 3 weeks before lambing, whereas 5 mg. Se (as sodium selenate) given once orally reduced the number of peri-natal deaths of lambs caused by white muscle disease; administration of 1 mg. Se orally to lambs 2 to 3 weeks after birth almost completely prevented the disease and 300 mg. α-tocopherol gave some protection. In a large number of field trials it was found that oral administration of three 5 mg. doses of Se (as sodium selenate) to lambs 5 to 8 months of age accelerated weight gains and reduced mortalities on farms where unthiftiness in weaned and unweaned lambs was high. This unthriftiness ("hogget ill-thrift") is an entity which commonly occurs in early autumn in weaned lambs grazing lush pasture and is an important cause of economic loss in the New Zealand sheep industry. Later reports (N.Z. Dept. Agric. Rep. 1959-60) indicate that administration of 5 mg. Se at monthly intervals to ewes from one month before tupping to just before lambing, greatly increased the lambing percentage, decreased the number of barren ewes and eliminated congenital white muscle disease on farms where there is often a concomitant barren ewe problem as well as congenital white muscle disease.

Oral doses of small amounts of selenium prevented muscular dystrophy in calves in areas of North Scotland (Sharman, Blaxter & Wilson, 1959) where earlier work (Blaxter & Sharman, 1953; Sharman, 1954) had demonstrated that relatively large doses of α-tocopherol were necessary to prevent the disease. A later report (Blaxter, McCallum, Wilson, Sharman & Donald, 1961) confirmed that administration of selenium by oral or subcutaneous routes were effective in reducing the incidence of muscular dystrophy in calves and that α-tocopherol given orally was slightly but not significantly less effective; a single injection of 15 mg. Se as sodium selenate within a few days of birth or injection of 5 mg. selenium at 3-week intervals from birth afforded considerable but not complete protection in two groups of 51 calves; 5 mg. selenium by mouth at 3-week intervals from birth afforded complete protection to a third group of 51 calves.

This brief review indicates some of the diverse effects of selenium—harmful when too much is present in the diet and beneficial when very small supplements are added to rations which cause certain disease entities. As yet it is too early to say whether these latter rations are deficient in selenium since the determination of trace amounts of selenium is difficult and satisfactory analytical methods have only recently been worked out. It appears too, that there may be variations in the optimal requirements of selenium relative to its various physiological effects, and these will have to be determined for different classes of stock.

It is obvious also that selenium is a toxic element since small amounts in the food may cause chronic poisoning. However, Schwarz (1960) has pointed out that the minimum chronic toxic dose of selenite-selenium is approximately 300 to 400 μg. per 100 g. of diet (3 to 4 p.p.m.) and if this level is compared with that which protects against Factor 3-deficiency, then selenium is relatively not more toxic than many other dietary constituents. The ratio between effective dose and toxic dose is of the order of 1 to 100 which compares favourably with the therapeutic indices of amino-acids, salts and almost all other important nutrients (Schwarz, *loc. cit.*). But no one would deny that considerable caution should be used concerning the therapeutic or prophylactic use of selenium and that the safest method of supplementation would be by parenteral administration. In New Zealand the use of the element has, by regulation, been brought under professional control and in the United States of America its use is regulated under the Food Additives (Delaney) Amendment of the Pure Food and Drug Act. It would therefore seem sensible that steps should be taken in this country to prohibit the use of selenium in mineral mixtures, as an additive in compound foodstuffs, or as a fertiliser for top-dressing purposes. These precautions, however, should not hinder investigations into its possible beneficial effect in livestock in Britain.

## Conclusions

Cobalt has not been included in this review because only two years ago Owen (1959) discussed at a B.V.A. Congress the comparative metabolism of this element and referred to methods of administration, and because, with reasonable care, the chance of harmful effects from overdose appear to be slight.

Sufficient evidence has been presented, I hope, to indicate the inter-relationships and complexities of metabolism of some of the commoner minerals frequently used in mixtures and added to pelleted feeds. I hope, too, this discussion will not only provoke more thought before recommendations are made for use of mineral mixtures as insurances against possible but undiagnosed deficiencies, but

also provide a realisation that a balance or imbalance of inorganic elements can have a profound effect on the metabolism and health of the animal.

On the evidence available and reviewed, the two elements which, in excess, appear to be potentially most harmful are calcium and copper. There appear to be sound reasons why recommendations for the administration of copper to ruminants should be limited to scientific advisers and in particular to the veterinary profession who have facilities for making accurate diagnoses and administering therapeutic but non-toxic doses.

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## The Speaker's Introduction

**The Chairman, Mr. H. F. Hebeler,** in introducing the author, said that there could be few people not actually in the veterinary profession but closely connected with it who were better known to members of the Association and to members of the veterinary profession than Dr. Ruth Allcroft. Since she joined Dr. Green when he started the Biochemical Department at Weybridge in 1932, she had done a great amount of work of direct interest to veterinary surgeons, particularly those in general practice. They had reason to be grateful for the many contributions which had been received from her before.

**Dr. Ruth Allcroft** said that she had not attempted to define the mineral requirements of farm animals in this paper. At the present time she did not think that such a definition was possible, firstly because of the general lack of agreement on, or knowledge of, animal requirements for different classes of stock during the phases of growth, reproduction and lactation; and secondly, because modern methods for increasing production imposed new metabolic and nutritional requirements which had not yet been worked out.

She said that her aim had been to attempt a brief discussion of some of the practical aspects of the inter-relationships and actions of minerals in common use as mixtures for voluntary consumption, or for mixing with compounded feeding-stuffs. The discussion was to be limited to a few aspects which she thought needed emphasis at the present time, and these she would attempt to illustrate with slides.

Dr. Allcroft proposed to begin with copper, because she thought its metabolism and inter-relationships with other compounds to be among the most complex, and also because it did not seem to be appreciated that in ruminants, and particularly in sheep, the margin between enough and too much copper was small. It was also almost impossible to define an optimum dietary copper level for sheep and cattle, since symptoms which are caused by a genuine deficiency of copper can occur on diets containing an apparent abundance of copper. Conversely, a ration might contain an apparently normal amount of copper and yet permit an excessive accumulation in the tissues, leading to toxicity and death.

Two dietary components which are known to affect copper metabolism in sheep and cattle, are molybdenum and sulphate. There is a reciprocal antagonism between molybdenum and copper, and the inorganic sulphate content of the diet can influence the limiting effect of molybdenum on liver copper storage. This was demonstrated by Dick in Australia by experiments on stalled sheep. The speaker had prepared a diagram summarising some of his reported results which she hoped would illustrate certain inter-relationships of these three dietary components which were referred to in the text of her paper.

Dick suggested that some of the discrepancies in results reported from Australia and Britain, such as the occurrence of swayback and of copper deficiency in cattle on pastures of apparently normal copper and molybdenum contents, might be caused by the different intakes of inorganic sulphate under the conditions for which the observations were recorded. But analysis of many pasture samples had shown that occurrence of copper deficiency in cattle and sheep in Britain could not be explained in this way. There appeared to be ample sulphate present in all our herbage to allow any molybdenum present to exert its limiting effect on copper storage. There would therefore appear to be other as yet unknown factors which interfere with absorption or utilisation of copper in cattle. Because of the complexity of copper metabolism in sheep and cattle, it was evident that it was not possible to predict the probable copper status of animals from chemical examination of samples of feeding-stuffs or of soils in this country, except perhaps in obviously "teart" areas.

Since the liver is the chief organ for storage of copper, the copper content of the liver of most species reflects the concentration of copper in the diet except where interfering factors cause a conditioned deficiency. Beck (1956) has shown that in many mammalian species the copper intake can vary within fairly wide limits without a corresponding change in liver copper concentration. But sheep and cattle differ in this respect, and the concentration of copper in their livers varies with the intake, even within the range of dietary copper which could be considered as normal.

Beck also showed that there is a marked species difference in the normal range of copper in the liver as well as an appreciable individual variation which is common to all species. He found that the liver copper concentration of normal adults of most species usually lies between 10 to 50 p.p.m. on a dry matter basis with a high proportion falling between 15 to 30 p.p.m. But a few unrelated species have very much higher liver copper values ranging between 100 to 400 p.p.m. Among these are included the sheep, cow, duck, frog and some species of fish.

Dr. Allcroft had prepared a diagram from data reported by Beck and by Cunningham, and also from her own data, which she hoped would illustrate these marked species differences and emphasise that sheep and cattle should be considered as a special group.

Beck suggested that the high liver copper level characteristic of some species was due, not to a higher intake of copper or to a greater absorption, but to a lesser ability to restrict the storage of copper in the liver and to excrete stored copper. This applied particularly to sheep, which are very susceptible to copper poisoning. On the other hand, some species are extremely tolerant to high doses of copper; this group including the rat and domestic fowl. The pig is also relatively tolerant when compared with ruminants.

Dr. Allcroft then showed two slides, one summarising details of cases of copper poisoning in sheep with which they had been concerned recently. It showed that when the copper content of concentrate rations is above about 20 p.p.m., sheep of all ages may accumulate dangerously high amounts of copper in the liver. The other illustrated the very much greater tolerance of pigs to high dietary copper levels.

It is well known that many present-day rations for cattle and sheep supply very high intakes of calcium. In order to draw attention to some adverse effects of excessive amounts of dietary calcium she had tabulated some of the reported effects of high calcium intakes and these were shown in Slide 5. One of these effects was to reduce absorption of magnesium. This was illustrated by showing some results of a calf experiment carried out by Dr. Allcroft and her colleagues, in which it was found that hypomagnesaemia developed more quickly and severely on a ration providing an intake of calcium greatly in excess of magnesium. These results supported the postulation of MacIntyre and his colleagues that there was a common transport system for the absorption of divalent cations and suggested that the hypomagnesaemia of the milk-fed calf might be attributable partly to an abnormally high intake of calcium as well as to a low intake of magnesium.

The limiting effects of excess dietary calcium on absorption of magnesium and on growth rate made it pertinent to consider that many pelleted rations contain from 1 to 4 per cent. of a mineral supplement consisting of limestone, bone flour and salt and these may provide excessively high intakes of calcium for some classes of stock.

At a conference on "Mineral Mixtures in Compound Feeding-stuffs" held in London 11 years ago, one of the conclusions reached was that if mineral supplements were added to the diet in amounts small enough to be well

below the known toxic level, they could cause no harmful effects, and would merely act as an insurance against any possible deficiency. Dr. Allcroft thought that a reconsideration of this conclusion was overdue, and hoped that she had given enough evidence to indicate that a balance or imbalance of inorganic components of the diet could have a profound effect on the metabolism and health of the animal, and that mineral mixtures, instead of protecting against possible but undiagnosed deficiencies, might in some cases cause "conditioned" deficiencies, and in others cause excessive accumulation resulting in a condition of toxicity. She suggested that the profession should take a lead in advising on the rational use of mineral supplements, and that the administration of copper to animals should be limited to scientific advisers, and in particular to the veterinary profession, who have facilities for making accurate diagnoses and administering therapeutic, but non-toxic doses.

From what she had said that morning, she hoped no one would conclude that she thought mineral supplements were useless. She thought there was ample evidence that when used correctly, in circumstances where they were required, they could give very beneficial effects.

### The Opener

**Dr. J. A. A. Watt,** in opening the discussion, congratulated the author whose paper was of the standard that one had come to expect from her. She had succeeded in condensing a great amount of factual material into remarkably small space, and the paper provided a valuable work of reference of up-to-date material on a very difficult subject. He could do little more in opening the discussion than emphasise some points which seemed of great importance.

It was true to say that more "authoritative" nonsense had been spoken and written on this subject than on any other veterinary subject. Possibly the worst offence was the over-simplification of a very complex relationship and, as the author pointed out, knowledge was very inadequate on many points. Dr. Allcroft had emphasised the interrelationship between those minerals and the trouble which could follow rash interference. That point could not be over emphasised. The farmer, however, had been conditioned by advertising and publicity to look on minerals as a vague panacea for a multitude of ills, but in no case did he seem to be aware of the dangers of overfeeding some of those apparently harmless elements, for example, calcium, and the resultant conditioned deficiencies.

Of particular interest were the author's remarks on the effect of excess calcium on the availability of magnesium. Most mineral mixtures which were high in magnesium were also high in calcium. It would appear, therefore, that even an apparently satisfactory mineral mixture so far as magnesium content was concerned might conceivably have a reduced availability of magnesium. Thus in a magnesium mixture containing 25 per cent. magnesite the theoretical feeding level was 8 oz. per head per day—a fair quantity in itself As the other 75 per cent. contained a large proportion of calcium, the amount of magnesium might not in fact be sufficient. Many so-called antitetany mixtures contained less than that and the amount required to be fed was quite impractical.

No consideration of the mineral requirements of the cow could neglect to consider the type of sward being grazed. For example, if the animals were on a well-balanced pasture with a fair amount of clover then the calcium and P requirements should be met by the grazing. In such a case the most important need was to get the animal to consume the advised 2 oz. of magnesite without the bulk of other mineral constituents which in some mixtures would require a ridiculous quantity to be fed.

On intensively managed pasture where a high level of nitrogenous manuring had been carried out, however, thus wiping out the clover the Ca and P might not be adequate. Did Dr. Allcroft think there was any danger in withholding Ca and P supplements for the comparatively short time when the risk was greatest? Could the skeletal reserves take care of the deficiency of Ca and P without danger of, say, milk fever developing?

He desired to emphasise the point made by the author that stockowners—even knowledgeable ones—were rarely aware of the fact that the feeding of magnesium before exposure to risk was quite useless. It was in fact common practice to feed the magnesium until the animals went out to grass and then stop. Although the amount of calcined magnesite required to protect against tetany was well known, he had yet to see the necessary statement on a label "X ounces of this product contains 2 oz. calcined magnesite" which was the only criterion of any value and would enable the farmer to assess its worth.

With regard to the author's remarks on the difficulty of getting the correct dose into sheep and suckling cows, he had found that two-thirds of an ounce of calcined magnesite suspended in water could be given to a ewe without scouring developing. That had raised the serum magnesium to normal and it had remained up for several days. This procedure might be useful where feeding was difficult and an outbreak was developing.

The problems associated with copper supplementation and deficiencies were of serious importance in some areas. Dr. Allcroft pointed to several factors which could lead to erroneous conclusions from blood analysis. As the condition might affect animals of some value the possibility of liver samples was not always feasible except by biopsy. Could the author expand on what reliance could in fact be placed on low blood copper values as a diagnostic test?

The feeding of copper supplemented licks to sheep was, in his opinion, a practice to be avoided. Only by the administration of a direct dose could one ensure the amount of copper consumed. Deaths from copper poisoning could follow for a considerable time after supplement feeding had ceased, especially on a change of pasture or dosing with a copper supplemented anthelmintic—the author did not mention that factor—and outbreaks were still common in spite of considerable publicity. Here again many manufacturers did not seem to keep up to date with findings. For the prevention of swayback it would appear that copper glycine injection must be the method of choice if the undesirable side-effects could be overcome. No copper supplement should be administered without ascertaining the management, for example, dry feeding and even the dosing programme in the flock.

It was gratifying to see that the author suggested that selenium should not be allowed as an additive or constituent of a mineral supplement. It was rather surprising that it had not already been included by some manufacturer, and it would seem advisable for the profession to take some steps to prevent that happening while there was yet time.

It was true to say that many of the mineral imbalances and deficiencies were man made and changes in agricultural practice led to changes in food constituents. That presented the profession with a series of problems which were never static. Unfortunately the position was sometimes complicated and worsened by some of the substances foisted on stock-owners under the vague heading of minerals and measures of definite value were brought into discredit by quite unsuitable mixtures.

(Dr. Watt showed a series of slides illustrating some examples.)

He pointed out that the samples were by no means representative of the better mineral manufacturer, and he did not desire it to be thought that he did not consider that mineral food was absolutely essential under present-day husbandry. The examples shown were those of the type of product encountered when investigating diseases which one might tend not to pin down to mineral deficiencies when the farmer stated that he was feeding such and such a mineral.

Dr. Watt said he would like to see it made compulsory to publish the constituents of any mixture on the bag together with the makers' recommendation for feeding. That would enable the veterinary surgeon to include the mixture in his background material in many problems without the irksome delay of waiting for analytical results. It might also stop the marketing of some valueless rubbish. He made it clear that only a minority were responsible for that trouble, but that minority could be very important in areas where their sales were made.

### The General Discussion

**Mr. Cassidy** (Northwich, Cheshire) said that his business

was the manufacturing of mineral supplements. He congratulated the author on a common-sense approach to the subject. She realised that minerals were necessary, and she had pinpointed certain dangers which those in the business respected. As far as Dr. Watt was concerned, it was appalling to hear him say that he had not yet seen on a label how a supplement should be fed. There were several reputable firms in the business, and each bag of material they sent to the farmer contained a label setting out how it should be fed. In fairness Dr. Watt might reasonably have shown other supplements which he considered suitable. One of the supplements shown contained 6 per cent. magnesium, and of course the comment was how much was it necessary to feed in order to supply 2 oz. of calcined magnesite. It had not occurred to Dr. Watt that it might have been designed for stall feeding during winter. If a supplement containing 10 per cent. magnesium oxide, which is equivalent to 6 magnesium was added at the rate of 5 per cent. to the food, the contribution of magnesium oxide was in excess of 2 g. per lb. of concentrate which meant that the high yielding animal getting somewhere in the region of 22 lb. of concentrates was in fact getting 2 oz. of calcined magnesite daily. That was necessary, because it must now be agreed that the condition occurs not only during the early spring and autumn flush, but throughout the 12 months of the year.

The author rightly said that protection was achieved only when feeding magnesium. Therefore, Mr. Cassidy's opinion was that magnesium should be fed all the time. Dr. Allcroft had pointed out that a high intake of calcium interfered with utilisation of magnesium, and Mr. Cassidy pointed out that this was very often the result of the home-grown foods fed by the farmer. He suggested that this could be encountered by feeding magnesium.

The other odd thing was that Dr. Watt did not mention salt at all. He made a statement to the effect that minerals contained something like 75 per cent. of limestone flour. As far as manufacturers were concerned, that was rubbish. There would be at least 30 per cent. salt, not to mention a considerable content of dicalcium phosphate or sterilised bone flour. It was necessary to get the whole matter in true perspective.

**Professor T. K. Ewer** (Bristol) supported the author in her statement concerning the bad effect of excess calcium, particularly in stock intensively fed. He recalled the recent work of Smith and Taylor (*Nature*, 1961, **191**, 1,200) showing that in many rations fed to broiler fowls to-day there was well over 1 per cent. of calcium. Their work clearly showed that in those cases where more than 0.8 per cent. calcium was given there was interference not only with the uptake of other minerals but also with the utilisation of protein. The young chickens grew a great deal better, making more efficient use of their food and grading better with less calcium in the diet. He wondered whether some of the present-day trouble arose from the cheapness of minerals. Practitioners were very careful about the amounts of protein which they advised for various types of stock because it was expensive. Minerals were cheap, and in his view there was often a tendency to be careless about exact quantities to be included in a diet.

**Mr. P. J. Daly** (Ballinrobe, Co. Mayo) said that as a practitioner he must compliment Dr. Allcroft and Dr. Watt on their approach to the whole subject, and in emphasising the dangers which arose from the use and abuse of mineral supplements.

He was inclined to be conservative and to have a "wait-and-see" approach to some of the more modern developments which seemed at times to be a "vicious circle."

The abuses of mineral supplements and also antibiotic additives were, he felt, leading to many of the problems which were becoming more and more common, particularly bony enlargements and osteodystrophy in the highly "stuffed" Thoroughbred yearlings which might lead to disastrous results in the Bloodstock Breeding industry. He had discussed this problem with one leading practitioner in Ireland who was also perturbed.

One breeder he knew—who had bred a Derby winner and also a dual Grand National winner among many other classic horses—would not on principle feed any mineral or antibiotic supplements to his horses and felt that good grass, good hay and oats (bran, etc.) were all that were required. He refused to feed hay that was produced as a result of concentrated manuring.

Pertaining to farm management and high production from manuring, he was fully in favour of modern science but on no account would he recommend to any client that he should have all his farm manured at one time; neither would he recommend the application of "weedicides" to the whole farm simultaneously, because he felt that it was always advisable to have some old pasture available whereby the animals, by selective grazing, would be in a position to rectify the problem of mineral imbalance by natural means.

**Dr. P. S. Blackburn** (Hannah Dairy Research Institute, Ayr) said the statement was made during this discussion that hypomagnesaemia occurred throughout the year, and he would be interested to learn whether that was general. Did it, for instance, occur during winter feeding? In the Institute herd there was no fall in the levels of serum magnesium during the period of winter feeding.

## The Replies

**Dr. Watt,** in reply to Mr. Cassidy, said that he had been misquoted. He had not said that 75 per cent. of mineral mixtures consisted of calcium. What he had said was that 75 per cent. had a large proportion of calcium—25 per cent. to 50 per cent. of the whole must be a large proportion of the 75 per cent.

With regard to the 6 per cent. magnesium mixture, the illustrations which he gave were of minerals being fed in the spring when animals were at grass. Six per cent. of magnesium in a mineral mixture would require the feeding of 20 oz. of mixture to provide 2 oz. of calcined magnesite per day.

He had not said that he had never seen the mineral constituents written on the bag. What he said was that he would like to see "X oz. of this mixture contains 2 oz. of calcined magnesite." He had also said that he would like to see it made compulsory for the analysis to be on the bag. It was put on the bag by reputable manufacturers.

**Dr. Ruth Allcroft,** in reply, referred to the value of blood copper estimations for assessing copper status of animals, and said that copper deficiency was a condition usually affecting the whole herd or flock or a certain group of animals in a herd. Therefore, blood copper levels were of considerable help in assessing the copper status provided blood samples were taken from a representative number of animals in the group concerned. A blood sample from one individual member of a herd was comparatively valueless, as were only a few blood samples from a large flock of sheep, since there could be a 10-fold variation between sheep in any flock.

Regarding the occurrence of hypomagnesaemia in stalled animals during the winter, we know that it can occur occasionally under these conditions. For example, in one of our experimental herds, several cases occurred in stalled animals which we termed "chronic hypomagnesaemia." The interesting thing about it was that in spite of giving 2 oz. of calcined magnesite twice daily for a period of weeks, serum magnesium values remained low—between 1 to 1.5 mg. per 100 ml.—although clinical symptoms of hypomagnesaemia did not recur. Her view was that high magnesium supplements should not be fed to stalled animals as a routine, unless the veterinary surgeon advised it.

**The Chairman** said that the meeting had been both useful and stimulating. Two points came to his mind after hearing the discussion and having read the paper. The first was that if those in practice were to carry out Dr. Allcroft's recommendations to the full, the great interest which the Association had in the provision of further laboratory facilities would be even more necessary.

Secondly, the Association had for some time been working on legal arrangements which might be made to require just that which Dr. Watt thought so essential, that is, that where drugs were added for the treatment or control of animal disease, a full statement of those active constituents should be contained on the label on the bag.

He proposed that a hearty vote of thanks be accorded to Dr. Allcroft for her paper and to Dr. Watt for opening the discussion.

The vote of thanks was carried by acclamation.

**Clinical Note**

## A Case of Torsion of the Uterus in the Pregnant Cat with Fatal Haemorrhage

**J. W. Pankhurst**

**and**

**M. A. H. Newman**

*Buxton, Derbyshire*

*Introduction*: Haemorrhage as a complication to torsion of the uterus, is, to our knowledge, an unreported condition. In this case, as the uterus underwent rotation, one can visualise a primary occlusion of the veins without interrupting the arterial supply, resulting in a subsequent engorgement of the zonal placentae. This ultimately led to rupture of the capillaries causing a fatal haemorrhage. We venture to suggest that the endotheliochorial type of placenta common to the Carnivora, is more prone to such a rupture of the capillary bed.

*Subject*: Four-year-old queen.

*History*: The owner had returned home at midday, having seen the animal in apparent normal health at 10 a.m., and found the animal in much discomfort, crying continually and having difficulty in moving. She was due to kitten within a few days. There had been 4 normal litters previously.

*Examination*: The animal appeared to be very shocked. It was crying continually and unable to walk, although reasonably alert. The visible mucous membranes were very pale, and the temperature was subnormal at 99.4°F. The cat resented abdominal palpation, but at least 2 kittens were located.

*Diagnosis*: A tentative diagnosis of rupture of the uterus with subsequent haemorrhage was made.

*Prognosis*: Even while the examination was being conducted, the general condition of the animal worsened and it was necessary to give a very grave prognosis.

*Treatment*: 10 ml. of a 20 per cent. solution of purified bovine albumen* was immediately administered intravenously as a blood volume expander. No improvement occurred, and indeed the cat was by this time comatose. With normal aseptic precautions, a midline laparotomy was commenced under local anaesthesia. The left uterine horn was immediately exposed. It appeared engorged and abnormally dark red. There was a torsion about its longitudinal axis; the torsion having occurred about the extreme proximal and distal ends of this horn. It was easily corrected by rotating it a full 1½ times, but unfortunately the animal died at this stage of the operation.

Post-mortem *examination*: The right uterine horn was quite normal and contained 1 foetus with no placental detachment. The left horn contained 2 foetuses and was enlarged, turgid and a dark red in colour. On incising the organ large quantities of blood were found between the endometrium and foetal membranes. Placental separation had occurred, and the maternal attachment was especially engorged, with large blood clots firmly adherent to its capillary bed. The allantoic and amniotic fluids were normal and contained no blood.

It may be of interest to mention that this animal's mother was a ginger queen with a history of abnormal kittenings, but the writers are unable to correlate this with a presumably physical condition.

* "Alboven," C. J. Hewlett Ltd.

# Current Literature

### BOOK REVIEWS

**Breed Improvement in Cattle Breeding.** By E. A. NOVIKOV, D. I. STARTSEV, & E. A. ARZUMANIAN. U.S.S.R. Publishing House for Agricultural Literature, Moscow, 1950. Translated by Birron, R. Farkab & M. Paenson, 1960. Published by the Israel Program for Scientific Translations, 1960.

The first part of this book is devoted to the principles of breed improvement in cattle breeding; the second to the performance of the 33 breeds of cattle in the U.S.S.R., breed by breed, and also to the yak and buffalo; giving some idea of the methods used and the results achieved up to the year 1948.

The book appears to be intended for the managers of state co-operative farms, and possibly of breed improvement farms too.

It gives some idea of the organisation of Soviet cattle breeding and of regional standards of husbandry. The importance of an increased plane of nutrition is emphasised repeatedly. According to some of the records it needs to be.

Basically the same principles of good husbandry are recognised in the U.S.S.R. as here—but there appears to be no shortage of labour.

The problem of lowered butterfat percentage is recognised when milk yield is increased, especially when Friesian blood is introduced. Little work as yet has been done to improve specialist beef production.

The methods used for breed improvement are the classical ones of line breeding, grading up and cross-breeding. Despite the use of artificial insemination, few bulls have records of more than 10 to 15 daughters. This insufficiency of numbers lessens the value of the tables of records. Production records above a minimum standard are now required for entry into any Herd Book so this fault may be rectified in the near future.

This book can be delved into by anyone interested in cattle breeding or cattle husbandry in the U.S.S.R.,

to confirm that no revolutionary methods had been introduced up to 1948.

**Flow Properties of Blood and Other Biological Systems.** Edited by A. L. Copley and G. Stainsby. Pergamon, 1960. 75s.

This is an account of the Proceedings of a conference held jointly by the Colloid Committee of The Faraday Society, and The British Society of Rheology. It contains about 40 contributions from current research on a very wide range of biological materials, from blood to protoplasm, deoxyribonucleic acid, mucus, muscle, milk and fish. The articles are presented by an almost equal variety of scientists, physicists, physiologists, haematologists and physicians, though not a veterinarian amongst them. They are all commonly interested in rheology, the science of flow and deformation of matter.

The book is likely to appeal to the biorheolobist or to the haemotologist who has time to practice or to read some fundamental research. For him there is a pleasing mixture of theory and practice; an introduction to rheology, some physical research with mathematical support, some papers on clinical aspects and a section on instrumentation.

The veterinarian may find some general interest and background here, but in his preoccupation with practice there is little of direct help. Three papers only are concerned with biological materials from domestic animals, one on cow's blood coagula, one on the coagulation of milk and one on bovine cervical mucus. These deal with physical properties of the materials with no immediate connexion with veterinary problems.

The book is extremely well produced, though rather expensive.

**The Biochemist's Handbook.** Edited by Cyril Long, M.A., B.SC., D.PHIL., F.R.S.E. Published by E. & F. N. Spon Ltd. Price 168s. net.

The production of reference books seems to us—thinking immediately of Beilstein—a typically German activity, though as the demand from English-speaking scientists has increased, the Americans have filled the gap. It is pleasant, therefore, to see a handbook with a distinctly British flavour in a subject which owes so much to pioneers in this country. Although the 170 or more contributors—all well-known in their own fields—have been drawn from all over the world, about half come from this country.

There are 1,125 pages of facts and references and a useful index of 65 pages, clearly printed on good paper and nicely bound. Can one do more with such a heterogeneous mass, having no style or theme, than indicate its scope and usefulness? It is certainly not possible to assess the accuracy of its information, for there is so much of it.

Six sections deal with chemical data (203 pp.), enzymes (328 pp.), metabolic pathways (106 pp.), chemical composition of animal tissues (300 pp.) and of plant tissues (124 pp.), and physiological and nutritional data (66 pp.).

Chemical data—mainly inorganic and physical, as many handbooks on organic chemistry are available—includes details of isotopes, analytical standards, ionic matters (buffers, indicators, pK's, Eh's), manometry, spectroscopy, chromatology. The enzyme section, after an introduction of theory, summarises the occurrence, preparation and properties of about 300 individual enzymes. The 24 major metabolic pathways range from the familiar tricarboxylic acid cycle to those more recently discovered, such as the biosynthesis of sterols, each clearly illustrated by formulae, equations and diagrams. This is the core of biochemistry where further expansion is envisaged; already it is itself practically a text-book of biochemistry. Data on chemical composition, largely tabulated and less readable, contains a bewildering amount of information too widely diverse to summarise. The section on plant products is unusual but welcome and ends with data on bacteria, yeasts and viruses. Physiological and nutritional data deal mainly with hormones, some chemical pathology, calories and food.

Veterinarians might favour a more conscious emphasis on data about domestic animals. An introductory table on vital statistics, for example, lists only man and laboratory animals, and calorie requirements and food tables relate mainly to man; nevertheless as the contributors include many who are interested in animals, an agreeably large amount of data on animals can be found.

Such compilations must lack homogeneity; in the main this lack is not obtrusive though occasionally it is marked: 3 pages on gas chromatography containing 5 tables contrast with 34 pages on paper chromatography, packed with information on theory, techniques and uses, contributed by one of its inventors. The editors mention that not all the promised articles arrived and this probably explains the relatively slender information on an especially important development.

The articles are often written in an informative and readable way and it is impossible to browse without lighting upon something of interest—the hereditary haemoglobinopathies, the structure of viruses, the conversion of cholesterol to steroid hormones, penicillinase, histochemistry. This would hardly justify the purchase of so expensive a book by a busy practitioner, though for anyone in contact with biochemistry or chemical physiology the book would be invaluable and certainly no library should be without it.

**A Short History of Veterinary Medicine in America.** By B. W. BIERER. Published by Michigan State University Press.

History on the whole is very dull, being largely a series of endless common-place incidents. But events applicable to a particular story, when picked out like the pieces of a jigsaw and fitted into a picture, assume reality and significance.

Here we have a very natural story of evolution, created by the natural impact of events upon the minds of human beings, bringing forth both good and evil, though eventually in this particular case, more of the former.

To those of us in the profession, it is of extreme interest to trace the changing relationship of man and animals all through the ages: seeing how superstition gave place to reason as the works of Hippocrates and Galen superimposed themselves on those of the old

Arab scientists, and how the veterinary art, especially applied to the horse, was highly developed from the elemental contact of man and his animals because of his need of them for transport and food.

The European veterinary school of course, starting with that at Lyon, in 1762, superseded the development of the same on the American continent. In the latter, it is interesting to trace the stirring of conscience aroused by the economic impact of disease, leading eventually to the provision of facilities for control. The United States began as an almost exclusively agricultural nation; so it was to be expected that the veterinary art was born as a result of the deliberations of various agricultural societies which first came into being for the promotion of agriculture.

The great characters of the age all receive in this book their due appreciation; amongst them are such men as Judge Peters (1770-1848), and Benjamin Rush (1746-1813). Other ecents of signfiicance are the opening of the school of veterinary medicine in conjunction with the medical department of the University of Pennsylvania in 1886, and the appearance on the scene of William Youatt (1777-1847), joint editor of *The Veterinarian*, who was widely known in America, his works being sold by the thousand. Some of his lectures were printed in the *Farmer and Gardener*!

The struggles and disagreements over the causes and control of plagues make interesting reading, and carry their lesson for those to-day engaged in scientific enquiry. There was in those days more justification for dogmatism and assumption, and even Gamgee (1831-1895) went astray in his attempt to explain Texas fever by ridiculing the tick theory. Salmon was eventually largely responsible for establishing the relationship between the tick and the infective agent. The struggle to establish the origin of hog cholera and the place of *Bacillus suis* (*S. cholerae suis*) in its correct perspective all make refreshing reading.

As the author rightly states, it does one good when faced with problems to-day to recall the struggles and hardships the early investigators went through to enable us to achieve our present status.

**Pig Records. Parts I and II of Official Scheme. Period II—October 1st, 1959-March 31st, 1960.** Pig Industry Development Authority.

One of the most attractive features of this enlightening publication is the presentation of a critique of the evidence alongside each table, though assimilation of the data might perhaps have been assisted further by presenting it, where suitable, in the form of histogram, frequency curve or such-like diagramatic method. Table 4, for example, lends itself particularly to a "distribution curve" form of presentation This view is perhaps encouraged by the fact that publications of this sort are read by the converted and shunned by those who perhaps most need enlightenment.

"A scrutiny of the tables gives very much food for thought. The pre-8 weeks losses are now higher (at 25 per cent.) than they were before the war (18 per cent.)" The veracity of the statement that 65 per cent of litters had *no* pigs born dead must be accepted although practical experience would raise a momentary mental query. Over 82 per cent. of the litters averaged under 130 lb. liveweight at 3 weeks; and Table 13 in general makes for very sorrowful reading. The number of piglets born alive in relation to the number of still-births seems to provide a good guide as to whether an animal is worth retaining for breeding. It has been stated that any sow which farrowed a small litter with a high number of still-born pigs should be considered for culling—particularly if this has happened with a previous litter.

There is a school of thought that believes it to be a fundamental fallacy to speak of the number of piglets born and the farrowing index as determining the success of a pig enterprise. Economically, apart from weight, what interests the producer is the number of pigs reared for sale per annum.

The report, like any other, can be viewed from many angles; but it provides valuable basic information and will repay careful study. If there is one thing which perhaps it was not intended to show, it is that, in Scotland and in the north, pig keepers know more about pig production than they do in the rest of the country!

## ABSTRACTS

**The Ferrophagous Bovine.** Annotation. *Lancet*. March 18th, 1961. P. 603.

This annotation, after quoting records from the United States of the incidence of traumatic peritonitis and pericarditis, goes on to mention a prophylactic method now parctised by an American veterinary surgeon. All young cattle are given orally a small cylindrical magnet which remains in the animal's stomach throughout life. It is claimed there has been a spectacular drop in the number of "wire" operations—formerly about 200 a year—which this American veterinary surgeon has had to carry out!

**Microbiological Studies on a New Broad-Spectrum Penicillin, "Penbritin."*** ROLINSON, G. N., & STEVENS, SHIRLEY (1961). *Brit. med. J.* July 22nd, 1961. Pp. 191-6.

"Penbritin" (B.R.L. 1341) is a new penicillin prepared from 6-aminopenicillanic acid. It is acid-stable and is active against a wide range of Gram-positive and Gram-negative bacteria.

Activity of penbritin against Gram-negative bacilli is similar to that of tetracycline and chloramphenicol.

Penbritin is slightly more active than benzylpenicillin, tetracycline or chloramphenicol against *Salmonella* species and *Haemophilus influenzae*. It is more active than tetracycline against the pyogenic cocci, and only slightly less active than benzylpenicillin.

Penbritin is not stable against penicillinase and therefore is not active against penicillin-resistant staphylococci or other penicillin-producing organisms. The activity of penbritin is not greatly affected by the presence of serum. Against certain organisms

* Penbritin is the registered trade mark of Beecham Research Laboratories Ltd.

it is more active at slightly acid *p*H than at higher *p*H values. Penbritin is highly bactericidal. Emergence of resistant strains develops stepwise in the typical penicillin manner.

**"Penbritin"—A New Broad Spectrum Antibiotic. Preliminary Pharmacology and Chemotherapy.** BROWN, D. M., & ACRED, P. (1961). *Brit. med. J.* July 22nd, 1961. Pp. 197-8.

Penbritin is an effective non-toxic oral penicillin possessing a wide stratum of activity. Animal studies indicate that it is better absorbed and gives more prolonged blood levels than penicillin V and phenethicillin. Its effectiveness against infections due to staphylococci and streptococci is equal to that of the existing oral penicillins.

The activity of penbritin *in vivo* against infections due to Gram-negative organisms is considered to be greater than that found with tetracycline and chloramphenicol.

**Absorption and Excretion of "Penbritin."** KNUDSEN, E. T., ROLINSON, G. N., & STEVENS, SHIRLEY. (1961). *Brit. med. J.* July 22nd, 1961. Pp. 198-200.

"Penbritin" is well absorbed when given orally to the human subject; some 30 per cent. of a given dose is excreted in the urine within 6 to 8 hours of dosing.

Studies of the relative value of single and multiple dose techniques suggested the following dosage regimen for human patients.

For the treatment of infections due to Gram-positive organisms or those due to *H. influenzae* 250 mg. every 6 hours. For infections of the urinary tract 250-500 mg. every 6 or 8 hours; a high concentration of penbritin is obtained in the urine. In the treatment of infections due to Gram-negative organisms, other than those in the urinary tract, 750 mg. or more at 8-hour intervals may well be required.

**"Penbritin": An Oral Penicillin with Broad-Spectrum Activity.** STEWART, G. T., COLES, H. M. T., NIXON, H. H., & HOLT, R. J. (1961). *Brit. med. J.* July 22nd, 1961. Pp. 200-6.

"Penbritin" has a bactericidal action compárable with that of benzylpenicillin on pyogenic cocci and on a wide range of coccal and bacillary pathogens.

It is affected by penicillinase and is therefore inactive against penicillinase-forming strains of *Staph. aureus* and certain coliforms.

Given orally in doses of 550-100 mg. per kg. per day the new compound is freely absorbed, and maintains a bactericidal level in the plasma for 4 hours or more. It is rapidly excreted in very high concentration in the urine.

It is concluded that penbritin deserves a further trial as a bactericidal penicillin-like drug with the antibacterial range of the tetracycline.

[Abstractor's Note. "Penbritin" is the name of BRL 1341. BRL 1241 has the trade name "Celbenin" and is also known as Methicillin].

**The Relative Antibacterial Activity of Four Penicillins.** GARROD, L. P. (1960). *Brit. med. J.* September 10th, 1960. Pp. 1,695-6.

When an antibiotic with new important properties is discovered it is apt to be introduced into clinical use before the full range of its antibacterial activity has been ascertained. This is particularly true of penicillins because it has sometimes been assumed that their action is identical, or nearly so, with that of benzylpenicillin. Penicillin V (Phenoxymethylpenicillin) was not only introduced but widely used for 6 years before this assumption was shown to be incorrect. Phenethicillin (Broxil) introduced as another acid-resistant penicillin, which is better absorbed than penicillin V, shows similar differences.

The resistance of Celbenin (BRL 1241) to penicillinase places it in a place apart for the treatment of resistant staphylococcal infections, and clinical experience has confirmed its value for this purpose. When this infection is of a less serious nature, and treatment with celbenin is impracticable, the slower inactivation of Broxil (and to some extent of penicillin V) by staphylococcal penicillinase, recommends its use in preference to benzylpenicillin.

The place of the newer penicillin in the treatment of any other infections than staphylococcal is more doubtful. Benzylpenicillin exceeds all other penicillins in activity against all other bacteria (except 2 uncommon species of *Proteus*) the differences being often wide. The nearest approach to the activity of benzylpenicillin against important pathogenic organisms such as haemolytic streptococci and pneumococci is that of penicillin V which may, therefore, reasonably claim to retain its place in the oral treatment of sufficiently sensitive infections.

**Hand-Foot-and-Mouth Disease in Birmingham in 1959.** ALSOP, J., FLEWETT, T. H., & FOSTER, J. R. (1960). *Brit. med. J.* December 10th, 1960. Pp. 1,708-11.

An outbreak of mild infection in children characterised by vesicular lesions in the mouth and on the hands and feet occurred in Birmingham in the summer of 1959. A few of the patients also had a maculopapular rash on the buttocks. Coxsacki group A type 16 virus was isolated from vesicle fluid from the hands of one. The disease appeared to be similar to that described as occurring in Toronto in 1957.

G. F. B.

**Methicillin.** DOUTHWAITE, A. H., TRAFFORD, J. A. P., MCGILL, D. A. F., & EVANS, I. E. (1961). *Brit. med. J.* July 1st, 1961. Pp. 6-8.

Methicillin (Celbenin) is of proved value in the treatment of staphylococcal infections that are resistant to benzylpenicillin (penicillin G).

The present report deals with 46 human patients, all of whom had benzylpenicillin-resistant staphylococcal infections and underwent treatment with methicillin. The dosage of methicillin ranging from a minimum of 750 mg. three times daily to a maximum of 1 g. four times daily. No case failed to respond to methicillin.

The level of sensitivity *in vitro* of the staphylococci

obtained from these cases was between 2 and 4 μg. per ml. An exception was a coagulase-negative staphylococcus in which the sensitivity was 6.5 μg. per ml. An intramuscular injection of 1 g. methicillin gave a serum level of 2 to 4 μg. per ml. for only 2½ hours.

As 75 per cent. of the methicillin is excreted in the urine, probenecid was administered in order to judge its effect in blocking the renal tubular excretion of methicillin. If 0.5 g. of probenecid 4 times a day is added to the treatment the effective blood level of methicillin is maintained for 6 to 8 hours and the peak levels obtained in the serum are increased

Injections of methicillin are painful; the administration of lignocaine hydrochloride before injection reduces the pain considerably.

It would appear that, like benzylpenicillin, methicillin gains access to the cerebrospinal fluid only when a meningeal lesion exists.

**Hydroxyprogesterone Acetate: Use in Estrogenic and Progesterogenic States in the Bitch.** BEARD, O. C. *Small Animal Clinician*. **1.** 215.

The author reviews the literature and records his observations on the use of the drug on a limited number of clinical cases. Hydroxyprogesterone acetate acts centrally as an antigonadotropin, peripherally as a progestogen. It appears to be useful in postponing oestrus, and in terminating prolonged oestrus in the bitch.

R. C. F.

**A New Synthetic Penicillin PA-248.** WILLIAMSON, G. M., MORRISON, J. K., & STEVENS, K. J. (1961). *Lancet*. April 22nd, 1961. Pp. 847-50.

α-Phenoxypropyl penicillin (PA-248) is a new synthetic penicillin. Its potential therapeutic value has been assessed by determination of its antibacterial spectrum *in vitro*, in conjunction with measurements of serum levels after oral administration. PA-248 produces peak serum levels approximately 4 times as high as those of penicillin V and 20 per cent. higher than those of phenethicillin.

Correlation of these relative serum levels with *in vitro* results indicates that:

(1) the 3 oral penicillins will be equally effective against sensitive staphylococci; (2) PA-248 will be the most effective of the 3 oral penicillins against resistant staphylococci; and (3) PA-248 will be the most effective of the 3 oral penicillins in streptococcal infections.

Attention is drawn to the fact that the 3 oral penicillins are less effective than benzyl penicillin against gram-negative cocci and bacilli.

**Clinical Use of a New Synthetic Penicillin: PA-248.** NAGLEY, M. (1961). *Lancet*. April 22nd, 1961. P. 851.

Two groups of patients with respiratory infections were treated—one with α-phenoxypropyl penicillin (PA-248) and the other with penicillin V. The response in the 2 groups was identical.

α-phenoxypropyl penicillin was effective in 5 cases with penicillin-resistant staphylococci in the sputum.

G. F. B.

**A New Synthetic Penicillin.** DOUTHWAITE, A. H., & TRAFFORD, J. A. P. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 687-90.

A clinical trial of BRL 1241 (Celbenin), a derivative of 6-amino-penicillanic acid is reported. The drug was administered by intramuscular injection; the injections were painful and prolonged treatment caused local reactions. No serious toxic reactions were encountered.

The drug was successful in eradicating staphylococci in 13 cases of staphylococcal infection resistant to benzylpenicillin and other antibiotics.

**A New Penicillin (BRL 1241) Active Against Penicillin-Resistant Staphylococci.** KNOX, R. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 690-3.

Although a powerful inducer of staphylococcal penicillinase, BRL 1241 is not itself appreciably destroyed by it. Its activity against penicillinase-producing staphylococci is relatively unaffected by inoculum size, and its antibacterial action is unaffected by concentrations of cell-free penicillinase which completely inactivate high concentrations of benzylpenicillin, penicillin V and Broxil.

**Microbiological Studies on Sodium 6-(2, 6 Dimethoxybenzamido) Penicillinate Monohydrate (BRL 1241) in Vitro and in Patients.** STEWART, G. T., HARRISON, PATRICIA M., & HOLT, R. J. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 694-9.

BRL 1241 has a strong bactericidal action against *Staphylococcus aureus*, streptococci of group A, and other pyogenic cocci in concentrations of 1 to μg. per ml. Such concentrations can be attained in the serum in children with 4 intramuscular injections at a dose of 100 mg. per kg. per day. Two-thirds of this dosage is excreted in the urine unchanged within a few hours of injection, while a considerable proportion of the remainder is excreted in the bile.

**Absorption and Excretion of a New Antibiotic (BRL 1241).** KNUDSEN, E. T., & ROLLINSON, G. N. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 700-3.

Investigation on the absorption and excretion of BRL 1241 showed that a dosage of 1 g. of the sodium salt, 4 to 6 hourly by intramuscular injection would be satisfactory for therapeutic trials in adults. If given slowly by deep intramuscular injection BRL 1241 was no more painful than benzyl penicillin.

**Report on Clinical Use of BRL 1241 in Children with Staphylococcal and Streptococcal Infections.** STEWART, G. T., NIXON, H. H., COLES, H. M. T., KESSON, C. W., LAWSON, D., THOMAS, R. G., MISHRA, J. N., MITCHELL, M. EILEEN, SEMMENS, J. MARJORIE, & WADE, T. H. H. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 703-6.

BRL 1241 was used in treating 17 children with infections due to *Staphylococcus aureus* and 12 children with streptococcal infections.

In 14 children with staphylococcal infection and in 10 children with streptococcal infection, clinical improvement occurred together with elimination of the organism from the site of infection, though not always

in the case of *Staph. aureus*, from the nostrils of nasal carriers.

In the therapeutic doses used (100 mg. per kg. per day in 4 intramuscular injections) BRL 1241 caused discomfort at the site of injection.

**Treatment of Experimental Penicillin-Resistant Staphylococcal Lesions with BRL 1241.** THOMPSON, R. E. M., WHITBY, J. L., & HARDING, J. W. (1960). *Brit. med. J.* September 3rd, 1960. Pp. 706-8.

BRL 1241 is shown to be effective in the treatment of penicillin-resistant infections in mice. The results of treatment with the drug are compared with results obtained in the treatment of similar infections with antibiotics in common use. G. F. B.

**Control of Nasal Botfly in Sheep.** MILLER, J. H., JOHNSON, H. E., & STOUT, A. L. (1961). *J. Amer. vet. med. Ass.* **138.** 431.

Organic phosphoramidate (Ruelene. Dow Chemical Co.) was used in 2 forms for the control of oestrus evis in sheep and lambs. A concentrated liquid preparation and a wettable powder were the 2 forms tested, and the dose was calculated as 125 mg. per kg. bodyweight of active ingredient given by mouth.

Results as judged by both clinical assessment and by *post-mortem* examination showed effective control of the oestrus evis larvae and toxicity trials showed that up to 3 times the therapeutic dose could be given with safety. It is suggested that this parasite might be eliminated from an area by he use of this drug.

R. F. S.

# Divisional News

## THE WESTERN COUNTIES VETERINARY ASSOCIATION

The summer meeting of the Association was held at the Hotel Victoria, Newquay, on May 25th, 1961. Mr. G. Blaikley, the President, was in the chair. Twenty-eight members and 2 visitors attended. Ten apologies for absence were received. The minutes of the last meeting were read and signed as a correct record.

*Correspondence*

Letters from the B.V.A. with regard to the B.V.A.-R.S.P.C.A. agreement, nutrition chemists, broken needles in flesh of food animals, and representation on B.V.A. Council were read and commented upon.

A letter from Mr. R. H. James with regard to the L.V.I. appointment of an assistant was read and replied to by Mr. Cameron.

*New Members*

Mr. J. C. Hindson, Tygwyn, Hatherleigh, Devon; Mr. A. McK. Taylor, Ivy Dale, North Tawton, Devon; Mr. T. M. McHugh, Pentreve House, Bow, Devon; Mr. C. F. Cartwright, 14 Church Street, Modbury and Mr. G. A. Embleton, 43 Brownston Street, Modbury were nominated.

Messrs. Irwin, Attenborough, Webster and Reakes were elected unanimously.

*Honorary Member*

Mr. J. A. Dall proposed that Mr. C. E. Perry, of Bristol, should be made an Honorary Member of the Western Counties Veterinary Association. This was seconded by Mr. MacKellar and carried unanimously.

*Papers*

Mr. J. Cameron presented a paper on foot-and-mouth, illustrated by colour slides. A vigorous discussion followed in which Messrs. Ayliffe, Pettett, Willing, Dall, MacKellar, Forrest, Alexander and White took part.

Mr. A. D. Campbell presented a paper on swine fever, illustrated by slides. He dealt with *post-mortem* lesions, and also discussed the eradication scheme. This stimulated a vigorous discussion in which Messrs. MacKellar, White, Orfeur, Fincham, Pettett, Turnbull and Ayliffe took part.

Mr. R. H. James proposed a vote of thanks to both speakers and congratulated them on their excellent papers.

Tea was taken, after which the future relationship of the Cornwall Clinical Club to the Western Counties Veterinary Association was discussed. Mr. L. F. Perkins proposed that there should not be any alteration to the rules of W.C.V.A. to make Cornwall a branch at present, and that it would be better to wait until the effect of the reduction in numbers of B.V.A. council representatives was seen. This was seconded by Mr. Cameron. A vote was taken and the proposition was defeated by 20 votes to 4 with 4 abstentions.

Messrs. James and Turnbull both spoke on the special needs of Cornwall in this matter, and it was decided that measures should be taken to make Cornwall Clinical Club a branch of the Western Counties Veterinary Association.

Unfortunately, due to the late hour, the discussion had to be postponed and it was resolved that it should be brought up at the next meeting.

## THE YORKSHIRE DIVISION

A general meeting was held on April 28th, 1961, in the Royal Station Hotel, York. The President, Mr. P. Y. Stead, was in the chair. There were present 36 members and 5 guests.

*Minutes*

The minutes of the A.G.M. held on Februray 10th, 1961, were read and signed.

*Correspondence*

A letter was read from the B.V.A. about the Harry Steele-Bodger Memorial Prize. Reference was made to the provisional arrangements made for the B.V.A. Congress at Scarborough, in 1962. Nutrition chemists of N.A.A.S. were reported as being willing to address Divisions on the nutrition of farm animals. Poultry refresher courses were commended. A new B.V.A.-R.S.P.C.A. agreement had come into effect on April 1st, 1961.

*Membership*

Mr. D. Christie submitted his resignation which was accepted with regret. Mr. C. T. MacRae, and Mr. J. M. Potts were elected to membership.

*Swine Fever Vaccination Scheme*

It was decided, in view of the letter from the B.V.A. and developments in national policy for the control of this disease, that it would be better not to promote this scheme.

*Guide to Fees*

Council set up two sub-committees to advise on the large- and small-animal sections.

*Future of the Society*

As a matter of explanation, the President stated that the Officers were seeking to find the best way for the Society to fulfil its services to members. Reference was also made to the method of formation of the B.V.A. Council.

*Next General Meeting*

The secretary was asked to make arrangements with the Parkway Hotel or the Metropole, in Leeds, according to the facilities available.

*Address by Dr. D. Poynter*

Dr. D. Poynter gave his paper on *The Control of Husk*. He illustrated his talk with a film and slides. Clinical aspects were dealt with by Mr. Peacock. Afterwards, Mr. W. H. Parker spoke on *Aspects of Diagnosis and Treatment*. The subject was enjoyed by the audience; and afterwards there was a very active discussion. A vote of thanks was proposed by Mr. J. L. Crooks, seconded by Mr. E. V. Fawell, and accorded by all those present.

# News and Comment

## B.V.A. JANUARY COUNCIL AND COMMITTEE MEETINGS

Owing to the fact that the dates proposed for the B.V.A. January Council and Committee Meetings followed so closely on the holiday season and the meetings of the Royal College of Veterinary Surgeons, it has been decided to postpone the B.V.A. quarterly meetings by one week. Members are asked to note that the meetings will now be held on:—

Wednesday, January 17th

Thursday, January 18th, and

Friday, January 19th.

The Committee meetings will be held at 7, Mansfield Street, but the place of the Council meeting will be announced later.

## PIG PRODUCTION CONFERENCE

The need for inter-relationship in the pig industry in order to increase efficiency was discussed at a Glaxo Pig Production Conference held at Brighton on November 14th.

Dr. A. O. Betts of the School of Veterinary Medicine, Cambridge, discussed the technique of production of pathogen-free pigs by hysterectomy, and the future use of the piglets as "minimal disease pigs" in establishing "disease-free herds." In outlining the extent of this system in the United States he was able to give some indication as to the type of administration and legislation necessary if a Swine Re-population Programme was started in this country. If such a re-population programme were to be started then the veterinary profession would necessarily have to play an important part, firstly in the initial stages using the specialised techniques in the production of the pathogen-free pigs, and secondly in the "minimal disease herds" where advice on prophylaxis rather than treatment would be sought.

Dr. Betts also dealt with the common disease problems and their importance to the industry, referring particularly to piglet anaemia and the variety of infections associated with *E. coli*. Although the pig breeder has a multiplicity of drugs available for the prevention of piglet anaemia the disease still produces great losses to the industry. The obvious method of prophylaxis is by the use of vaccines; in certain cases these produce satisfactory results, but they have not been able to eliminate the diseases which are of great economic importance.

One of the speakers in the morning session, Sir Alick Buchanan-Smith, Vice-Chairman of the P.I.D.A., spoke on "Breeding for Optimal Production." He related the advances that had been achieved in the past few years to the more rapid progress that he felt could take place by utilising knowledge of pig performance. Although nutrition was discussed fully later in the conference by Mr. G. A. Childs, of Glaxo Laboratories, Sir Alick raised one point which had recently become an acute problem. This related to the greater efficiency of the boar as a food converter over that of the gilt and the castrated hog. Specialised feeding of young boars would no doubt become commonplace in the larger pig breeding units.

The final paper on the economics of pig farming was given by Mr. F. G. Sturrock, Director of the Farm Economics Branch, Cambridge.

## PERSONAL

### Births

BRIDGES.—On November 16th, 1961, to Barbara, wife of Gordon D. Bridges, B.V.M.S., M.R.C.V.S., of 6, Palace Gardens, Wiveliscombe, Somerset, a daughter, Lynne Catriona, a sister for Ann.

RANDLESOME.—On October 25th, 1961, to Menai, wife of Anthony G. C. Randlesome, B.VET.MED., M.R.C.V.S., Provost, Alberta, Canada, a son, Ian Douglas, a brother for Neil and Ellen.

SMITH.—On October 20th, 1961, to Rosemary, wife of Roderick J. Smith of Hampton Villa, Wool, Dorset, a son, Michael Craig.

WILSON.—On November 20th, 1961, to Noni (*née* Sapte), wife of Robert M. Wilson, M.R.C.V.S., of Chipping Norton, a son.

**Engagement**

HANSON—SEARLES.—The engagement is announced between David William Hanson, The Prince of Wales's Own Regiment of Yorkshire, son of the late Lt.-Col. F. A. Hanson and of Mrs. Hanson of Bighton, Alresford, Hampshire, and Patricia Anne, B.V.M.S., M.R.C.V.S., daughter of Mr. and Mrs. G. W. Searles, M.R.C.V.S., of Thodys, Alresford, Hampshire.

## R.C.V.S. OBITUARY

We record with regret the deaths of the following members of the profession:—

BROWN, Roger Harry, District Veterinary Officer at Nyeri, Kenya. Graduated London, July 4th, 1947. Drowned in the Kenya floods, November 19th, 1961.

SHANNON, James Aloysius, Captain, late R.A.V.C., 4, Idrone Terrace, Blackrock, Co. Dublin. Graduated from the Veterinary College of Ireland, Dublin, December 10th, 1913. Died in Sir Patrick Duns' Hospital, Dublin, aged 66, on October 23rd, 1961.

TRIGGER, William, of 6, Queen Street, Newcastle-under-Lyme, Staffordshire. Graduated London, August 30th, 1904. Died November 15th, 1961.

## COMING EVENTS

### November

27th (Mon.). EAST YORKSHIRE CLINICAL CLUB. Meeting at the Talbot Hotel, Malton, 8 p.m.

29th (Wed.). SOUTHERN COUNTIES VETERINARY SOCIETY. Meeting at the Polygon Hotel, Southampton, 7.30 p.m.

B.S.A.V.A. METROPOLITAN REGION. Joint Meeting with the Hounslow Veterinary Club, 7.30 p.m.

30th (Thurs.). WESTERN COUNTIES VETERINARY ASSOCIATION. Meeting at Agriculture House, Exeter, 2.15 p.m.

### December

1st (Fri.). SOUTH WALES DIVISION. Meeting at the Park Hotel, Cardiff, 2.15 p.m.

LAKELAND VETERINARY ASSOCIATION. Dinner Dance at the Old England Hotel, Windermere, 7.30 p.m.

ROYAL COUNTIES VETERINARY ASSOCIATION. Meeting at the Caversham Bridge Hotel, Reading, 2.30 p.m.

V.V.B.F. NORTH WALES DIVISION. Annual Dinner Dance in the Royal Lido, Prestatyn, 7.30 p.m.

2nd (Sat.). B.S.A.V.A. SOUTHERN COUNTIES REGION. Meeting at 50, Bridge Road, Cove, Farnborough, Hants., 7.30 p.m.

5th (Tues.). NORTH WILTS. VETERINARY CLUB. Meeting at the Goddard Arms Hotel, Swindon, 7.30 p.m.

6th (Wed.). A.V.T. & R.W. SCOTTISH GROUP. Meeting in the Assembly Hall at the University of Glasgow Veterinary Hospital, Bearsden Road, Bearsden, 2.30 p.m.

B.S.A.V.A. MIDLAND REGION. Meeting in Simon's Lounge, Grand Hotel, Leicester, 8.15 p.m.

B.S.A.V.A. KENT REGION. Meeting at the Great Danes Hotel, Ashford Road, Maidstone, Kent, 7.45 p.m.

B.S.A.V.A. REGION NO. 2. Meeting at the Hotel Metropole, King Street, Leeds, 8 p.m.

MIDLAND COUNTIES VETERINARY ASSOCIATION. Joint meeting with the Worcestershire Veterinary Club at the Castle Hotel, Worcester Road, Droitwich, 8 p.m.

7th (Thurs.). AYRSHIRE VETERINARY ASSOCIATION. Meeting in the New Building, Auchincruive, 7.30 p.m.

CENTRAL VETERINARY SOCIETY. Meeting at the Royal Veterinary College, Camden Town, N.W.1, 6 p.m.

8th (Fri.). WESTERN COUNTIES VETERINARY ASSOCIATION. Annual Dinner and Dance at the Rougemont Hotel, Exeter, 7 p.m.

13th (Wed.). NORTH OF ENGLAND VETERINARY MEDICAL ASSOCIATION. Annual Dinner Dance in aid of the V.V.B.F. at the Banqueting Rooms, Gosforth Park Race Course, Newcastle upon Tyne, 7.30 p.m.

## ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the date on which disease has been confirmed, followed by the postal address and local authority.

### Anthrax

November 14th, 1961. T. Broad, Bayfordbury Park Farm, Hertford, Herts. (Cattle.) HERTFORDSHIRE.

November 16th, 1961. R. H. Dutton, Old Marton Farm, Ellesmere, Salop (Parish: Ellesmere). (Cattle.) SHROPSHIRE.

November 16th, 1961. J. Andrews, Rowanstone, Crosshill, Maybole, Ayrshire (Parish: Kirkmichael). (Cattle.) AYRSHIRE.

November 16th, 1961. W. A. Webber, Lockridge Farm, Bere Alston, Yelverton, Devon (Parish: Bere Ferres.) (Cattle.) DEVONSHIRE.

November 16th, 1961. E. W. Pepper, Wyndmere Piggeries, Steeple Morden, Royston, Herts. (Parish: Steeple Morden). (Swine.) CAMBRIDGESHIRE.

November 17th, 1961. A. Kilmartin, Thornborough Farm, Kings Norton, Birmingham. Disease at: Woodwards Farm, Hollywood, Birmingham. (Cattle.) WORCESTERSHIRE.

November 20th, 1961. J. W. Norman, Great Lyewood Farm, Ardingley, Haywards Heath, Sussex (Parish: Ardingley). (Cattle.) EAST SUSSEX.

November 20th, 1961. K. J. C. Garrett, Old Farm, Templecombe, Somerset (Parish: Templecombe). (Cattle.) SOMERSET.

### Fowl Pest

November 14th, 1961. C. G. Nicholson, Follywood House, Easingwold Road, Huby, Sutton-on-Forest, York. YORK: NORTH RIDING.

November 14th, 1961. J. D. Hollingworth, Mayfield, Easingwold Road, Huby, Sutton-on-Forest, York. YORK: NORTH RIDING.

November 14th, 1961. A. K. E. Reeve, Crown Corner Cottages, Denham, Diss, Norfolk. EAST SUFFOLK.

November 14th, 1961. G. Goddard, Crown Corner Cottages, Denham, Diss, Norfolk. EAST SUFFOLK.

November 14th, 1961. D. Birkenshaw, Newlands, Easingwold Road, Huby, Sutton-on-Forest, York. YORK: NORTH RIDING.

November 14th, 1961. R. W. Watson, Chardwell Farm, Arkesden, Saffron Walden, Essex. ESSEX.
November 14th, 1961. C. J. Buckenham, Great Malgraves, Horden-on-the-Hill, Stanford-le-Hope, Essex. ESSEX.
November 14th, 1961. R. E. Archer, Brookside, Breckles, Attleborough, Norfolk. NORFOLK.
November 15th, 1961. H. V. Mills, 29, Elm Close, Great Barton, Bury St. Edmunds, Suffolk. WEST SUFFOLK.
November 15th, 1961. Mrs. L. Horner, The Homestead, Huby, Sutton-on-Forest, York. YORK, NORTH RIDING.
November 15th, 1961. Mrs. D. Galer, Meadow Farm, Garveston, Norwich, Norfolk. NOR 29K. NORFOLK.
November 15th, 1961. Mrs. M. Ellison, Berney, Little Gaddesden, Berkhamsted, Herts. HERTFORDSHIRE.
November 15th, 1961. E. Bliss, 58, Harthall Lane, King's Langley, Herts. HERTFORDSHIRE.
November 16th, 1961. Leavesden Hospital Management Committee (Farm Manager: W. D. Robinson), Leavesden Hospital, Abbots Langley, Watford, Herts. HERTFORDSHIRE.
November 16th, 1961. Mrs. E. Barker, Kirkmoors, Main Street, Huby, Sutton-on-Forest, York. YORK, NORTH RIDING.
November 16th, 1961. E. Humphrey, The Green, Polstead, Colchester, Essex. WEST SUFFOLK.
November 17th, 1961. W. H. Wheeler, 39, Cleveland Street, Cheltenham, Glos. Disease at: Staverton Poultry Farm, Staverton, Cheltenham, Glos. GLOUCESTERSHIRE.
November 18th, 1961. A. J. Black, Hilltop Poultry Farm, Hilltop Road, King's Langley, Herts. HERTFORDSHIRE.
November 18th, 1961. H. A. Smith, Pictoria Cottage, The Street, Burnham, King's Lynn, Norfolk. NORFOLK.
November 18th, 1961. W. C. Brown, Crown Lodge, Upshire, Waltham Abbey, Essex. ESSEX.
November 19th, 1961. J. H. Fisher, West Farm, Banham, Norwich, Norfolk. NOR 05X. NORFOLK.
November 20th, 1961. N. Harvey, Findenham Road, Kenninghall, Norwich, Norfolk. NOR 06X. NORFOLK.
November 20th, 1961. Messrs. G. A. Goymour and Son Ltd., The Grove, Banham, Norwich, Norfolk. NOR 05X.

**Swine Fever**

November 14th, 1961. T. E. Charles, Trent View, North Muskham, Newark, Notts. NOTTINGHAMSHIRE.
November 14th, 1961. J. Murphy, Catteshall Farm, Catteshall Lane, Godalming, Surrey. SURREY.
November 15th, 1961. P. Lawrenson, Scronkey Farm, Pilling, Preston, Lancs. LANCASHIRE.
November 15th, 1961. A. G. Sparrowhawk, No. 23, Little Woodcote Estate, Wallington, Surrey. SURREY.
November 15th, 1961. Mrs. D. M. Patterson, Clough House, Howdon Clough, Birstall, Leeds, Yorks. BOROUGH OF BATLEY.
November 15th, 1961. M. D. Gilder, Home Farm, Bishop's Cleeve, Cheltenham, Glos. GLOUCESTERSHIRE.
November 16th, 1961. W. N. I. Poupart, Stanyards Farm, Chobham, Surrey. SURREY.
November 16th, 1961. T. Cannon, 37, Coronation Estate, Upton, Pontefract, Yorks. Disease at: Piggeries, High Street, Upton, Pontefract, Yorks. YORK, WEST RIDING.
November 16th, 1961. E. C. Harris, The Bungalow, Tram Road, Caerleon, Newport, Mon. Disease at: Piggeries, Bulmoor Road, Caerleon, Newport, Mon. MONMOUTHSHIRE.
November 16th, 1961. F. Fisher, Railway Cottage, Ellerby Grange, Ellerby, Hull, Yorks. Disease at: Woodyard, School Corner, Old Ellerby, Hull, Yorks. YORK, EAST RIDING.
November 17th, 1961. P. E. Peckham, Leigh Cottage, 276, Woodcote Road, Purley, Surrey. SURREY.
November 17th, 1961. S. J. Seaman & Sons, Billingford Hall, Billingford, Dereham, Norfolk. Disease at: Old Hall Farm, North Elmham, Dereham, Norfolk. NORFOLK.
November 20th, 1961. M. Baker & Son, Church Farm, Leafield, Oxford. OXFORDSHIRE.
November 20th, 1961. E. Sankey, Rodenhurst Hale Farm, Rodington, Shrewsbury, Salop. SHROPSHIRE.
November 20th, 1961. R. D. Eaton, Plenty Farm, Llangennith, Gower, Swansea, Glam. GLAMORGAN.
November 20th, 1961. W. J. Pocock, The Dog Inn, Mappleborough Green, Redditch, Worcs. WARWICKSHIRE.
November 20th, 1961. L. M. G. Russell, Yerbeston Farm, Maidenwells, Pembroke. PEMBROKESHIRE.
November 20th, 1961. N. Tillotson, Low Farm, Goldsborough, Knaresborough, Yorks. YORK, WEST RIDING.

# Letters to the Editor

*The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.*

### V.V.B.F. Christmas Gifts

Sir,—For many years past the V.V.B. Fund has been able to send a small present of money at Christmas to aged and infirm members of the profession and widows who are in need of help. Of the latter, some have young children to maintain. In great measure, this assistance has been made possible by the generosity of your readers, who have forwarded donations for the purpose.

May we hope that this year we shall again receive a good response, so enabling us to bring some little extra comforts and happiness into these homes at Christmastide.

Please forward your donations, however small, payable to the *V.V.B.F. Christmas Fund a/c*, to the Secretary V.V.B. Fund, 29/31, Wright's Lane, London, W.8.

Should any readers prefer to send food parcels direct to our recipients, addresses will be gladly supplied.

Yours faithfully,
H. W. DAWES, *President.*
J. McCUNN, *Hon. Treasurer.*
J. J. DUNLOP, *Hon. Secretary.*
Victoria Veterinary Benevolent Fund,
College House,
Wright's Lane,
London, W.8.
*November 16th*, 1961.

### Control of Hypomagnesaemia

Sir,—Birch and Wolton (1961) have reported the prevention of hypomagnesaemia in cows on spring pasture which had been treated during the previous winter with as little as 50 lb. MgO (approximately ½ cwt. calcined magnesite) per acre. Although they state that "any conclusions from one year of an experiment such as this must be tentative" there is a danger that practising veterinary surgeons may be led to expect similar results under other conditions. It must, therefore, be emphasised that the type of soil is an important factor and will largely determine the response (as measured by increased content of magnesium in the herbage) to magnesium applications of this type.

It is to be expected that response will be inversely related to the base exchange capacity of the soil and would, therefore, be greater on light sandy soils than on heavy clay soils, and Collins' (1960) report would tend to support this. Also in collaborative trials in Northern Ireland (Todd, McConaghy & McAllister, unpublished) applications to a clay soil of calcined magnesite equivalent to 300 lb. MgO per acre and dolomite at varying rates up to 650 lb. MgO-equivalent per acre in winter, resulted in only limited increases in magnesium content of herbage in spring and did not prevent severe hypomagnesaemia in dairy cows grazing it. On lighter soils, however, response was proportionately greater and control of hypomagnesaemia was achieved.

It would seem, therefore, that the undoubted control that Birch and Walton achieved in this experiment was at least partly due to the fact that the soil was a sandy loam of low base exchange capacity where response would be maximal. That this could be repeated on heavier soils would seem doubtful.

These comments of course apply to the application of calcined magnesite in winter and subsequent uptake of magnesium by herbage when growth commences in spring. But Birch and Wolton suggest that part of the observed increase in magnesium content of the pasture may have been due to calcined magnesite adhering to the surface of the herbage, and it therefore seems logical to ask if all the extra magnesium required by the animals could be supplied *on* as distinct from *in* the herbage. With a view to providing some information on this question a number of trials have been carried out at this laboratory during 1961, both on ungrazed small plots and also on a field scale.

The results may be summarised as follows:—

(1) Ungrazed plots "dusted" with finely ground calcined magnesite at the rate of 100 lb. MgO per acre showed evidence of appreciable amounts still adhering more than 1 month later.

(2) Application of 50 lb. MgO (approximately ½ cwt. calcined magnesite) per acre restored serum magnesium levels to normal in a herd of suckler cows. Four cows had died during the previous 2 weeks and 5 out of 5 cows sampled showed moderate (2 cows) to severe (3 cows) hypomagnesaemia before the calcined magnesite was applied.

(3) In a herd of 15 suckler cows, 3 showed severe hypomagnesaemia (*i.e.* less than 1 mg. Mg per 100 ml.) and 4 moderate hypomagnesaemia (*i.e.* between 1 mg. and 1.4 mg. per 100 ml.) before treatment of the pasture with 25 lb. MgO per acre. One week later all showed normal serum magnesium levels.

In the latter 2 trials the calcined magnesite was applied with fertiliser distributors, and analyses of pasture even after heavy rain showed total magnesium contents of 0.3 to 0.6 per cent. of the dry matter. It should be emphasised that "dusting" pasture with small quantities of calcined magnesite is looked upon as treatment for that particular grazing only, with no residual effect, and the above results are presented merely to add weight to the suggestion that if small amounts of calcined magnesite are to be used, it might be better to apply them just before grazing rather than in winter.

Yours faithfully,
J. R. TODD.

Ministry of Agriculture for Northern Ireland,
Veterinary Research Division,
The Farm,
Stormont,
Belfast.

*November 14th*, 1961.

**References**

BIRCH, J. A., & WOLTON, K. M. (1961). *Vet. Rec.* **73**. 1,169.
COLLINS, F. C. (1960). B.V.A. Conference on Hypomagnesaemia. P. 115.

**Hand Rearing of Budgerigars**

Sir,—In view of the continued increase in the keeping and rearing of cagebirds, the following note on the value of yeast and $B_{12}$ supplements in the hand rearing of budgerigars may be of interest.

Last May I was approached by a colleague for advice on rearing 3 birds which had been thrown out of the nest by the hen.

They were from the 3rd clutch, and the previous breeding history of the hen, with the same cock throughout was as follows:—

1st clutch (6 eggs all hatched)—3 birds were found dead within the first week. The remaining 3 were hand reared from 3 weeks of age and all died. They had been thrown from the nest several times by the hen and replaced by the breeder and this may have been a contributory cause of death. Diet during hand rearing consisted of equal parts of Farex and Golden Glow full-cream milk powder mixed to a sloppy consistency with warm boiled water.

2nd clutch (4 eggs all hatched)—the hen reared 2 of these unaided.

3rd clutch, the following year (3 eggs all hatched); these birds were thrown out by the hen at 2 weeks. The same feeding was started and continued for 1 week at the end of which the birds were not doing well and advice was sought.

It was suggested that a supplement of entire B complex would probably be beneficial as any excess would be readily excreted and could do no harm.

Fresh dried yeast powder (1 per cent.) and sufficient $B_{12}$ to make the sloppy feed faintly pink was given by eye dropper to prevent the mixture falling on the neck and breast feathers, as this might lead to denudation and irritation followed by feather picking. At the end of a week on the supplemented feed the birds refused to be fed and started pecking millet seed. All 3 were reared.

The hen was given a yeast supplement and reared her next clutch of 4 without help (laid June 15th, hatched July 10th).

They were strong and fed themselves by pecking millet as soon as they left the nest. One was rather late learning to fly.

The early failures may have been partly due to the youth of the hen and consequent inexperience and partly due to the failure on the part of the cock to feed the hen while she was sitting and to take over the feeding of the young. The improve-

ment in the 2nd clutch (2 reared by the hen out of 4) tends to support this theory.

The food supplement, however, appeared to play a major rôle in the later success in hand rearing the 3rd clutch and the rearing of the whole of the 4th clutch by the hen.

Yours faithfully,
D. P. WATSON.

Royal Free Hospital School of Medicine,
8, Hunter Street,
London, W.C.1.
*November 10th*, 1961.

**Tick-borne Disease Control in Africa**

Sir,—I should very much appreciate the use of your correspondence column to discuss the advantages and disadvantages of a universal dipping policy for the control of tick-borne diseases of cattle in Africa. You will be aware that there is a divergence of opinion in the profession as to the advisability of instituting a dipping policy as a means of control of such diseases and in particular East Coast fever. It has been maintained that, in the absence of dipping, cattle acquire a lasting immunity to East Coast fever and that while there will be losses in calves these are by no means as great as might be the case if susceptible animals were to come into contact with the disease later in life.

We are committed in Nyasaland to the institution of universal dipping and in fact we are well on the way to achieving this aim, in that some 63 per cent. of the total cattle population are now dipped. It is of great importance to us to establish the reasons for the adoption of this policy so that it may be maintained into the future.

Our problem in this country, which has a low cattle population (356,000) and a high human population (2,750,000) is to integrate cattle with agriculture, and so to supply a valuable and vital source of food protein, while ensuring that a cheap source of fertiliser is available to improve subsistence and cash crops. Our cattle population is so valuable to us that it is very necessary that it should not be wasted by avoidable disease. The greatest cause of disease loss is tick-borne disease, and the cheapest way to control it is to institute dipping in arsenic on a regular weekly basis. At the same time we use the dipping tank as a means of supplying simple individual treatment and of inculcating improved principles of management. I might mention that our dipping scheme in the Central Province, where there has been a good coverage for many years now, has enabled us to obtain an offtake of 14 per cent. in slaughter stock while preserving an annual increase of 3 per cent. per year. That this increase is due to a vigorously pursued dipping policy is illustrated by the fact that in 1959 and 1960, when the tanks were ill attended for political reasons, the cattle population remained static. It is to be questioned whether such results could be obtained by any method which depended on the acquisition of an acquired immunity by unpredictable contact with the disease.

We also maintain complete tick control by dipping and spraying on our Livestock Improvement Centres. While we are aware that our problem is the future of susceptible improved stock in East Coast fever affected areas, we hope that by the time that we are ready to distribute such stock in adequate numbers we shall be able to insist on a high level of tick control as a prerequisite to the issue of stock to master farmers. Complete tick control is essential on a farm aiming at the improvement of livestock since it is important to eliminate any factor in the environment that might influence the selection of the stock. No conclusions arising from feeding trials or other investigations are possible in the presence of a haphazard disease factor.

The crucial point is the level of dipping efficiency which will ensure tick control. A factor in such tick control is the inducement to the average cattle owner to carry out the regulations, since in the present political context in Africa it is impossible to pursue any policy based on compulsion unless a majority of the people concerned are convinced of its efficacy. We have evidence that the ancillary services that we supply through the dipping tank, such as treatment of individual animals, management advice, and above all the means of selling hides and skins, do act as such an inducement and in themselves help to further the scheme by making the process more popular. We have always considered that weekly dipping of 80 per cent. of the cattle population is adequate to preserve control, and this is rather borne out by our figures, but I would appreciate the views of your readers on this very vital issue.

Finally I myself feel that the profession in Africa have achieved considerable success in controlling epizootic disease but that the big challenge now is the control of enzootic conditions. To us the dipping tank appears to supply the most efficient answer within our means, and the most obvious way by which we, as a profession, can develop and influence agricultural progress in primitive Africa.

Yours faithfully,
K. W. ASPINALL.

Department of Veterinary Services,
P.O. Box 90,
Zomba,
Nyasaland.
*November 16th*, 1961.

**Streptothricosis in Cattle**

Sir,—I was greatly interested by the article by I. Macadam (*Vet. Rec.* **73.** 1,039) in which he demonstrated that high humidity was associated with the healing of lesions of streptothricosis. The experiment described is a matter for congratulation in that it was well planned and executed, and yet I believe there is a flaw in it.

A characteristic feature of both streptothricosis in cattle and mycotic dermatitis in sheep is its persistence, infected animals showing lesions continuously for many months. In contrast the artificial infections produced by Macadam had all healed spontaneously within 30 days. In this respect, therefore, they cannot be regarded as typical of the disease as it occurs in nature and it seems most probable that the temporary lesions produced occur as a result of a massive infection of inoculated organisms which

do not settle down to produce a permanent lesion.

In working with mycotic dermatitis in sheep, we have found that whereas scarification consisting of one or a series of lines will only produce a temporary lesion, a scarification consisting of the removal of the superficial skin layers over a whole area, as with a razor, will allow the production of a lesion which will persist for at least 30 days in almost all cases. In dry weather there is a tendency for resolution after this period, but in damp, humid, but not necessarily hot, weather, a high proportion persists indefinitely and may spread.

Let us now consider what one would expect to be the effect of a humid and a dry atmosphere on the temporary lesion caused by a massive invasion of *Dermatophilus congolensis*. The initial lesion is a small papule which breaks and liberates a serous exudate. Under dry conditions, this exudate will form a hard crust, but under humid conditions it will not dry and on cattle skin may even be inapparent or only apparent during the first few days after inoculation. Let us now assume that under both conditions, humid or dry, the active outpouring of serous exudate from a temporary lesion lasts for an equal time. The hard, dry lesion will stick on the skin for a considerable time, but will eventually become loose at the base and with continued epidermal exfoliation will be cast. The lesion produced under humid conditions has never really developed such a good crust, those crusts which have formed will be rather smaller (Macadam noted lesions of 5 mm diameter) and are thus more easily shed than the lesions produced under dry conditions.

This line of argument is not a proof, nor is it necessarily true that the parts of it which are derived from work on mycotic dermatitis in sheep are applicable to cattle, but it is a suggestion which may be worth checking by further experiment.

Should the explanation be correct, it could be that, notwithstanding the shorter duration and lower incidence of temporary lesions in cattle kept under dry conditions, the incidence of persistent lesions could still be favoured by humid conditions or by actual rain.

Yours faithfully,
C. B. HART.

The Cooper Technical Bureau,
Berkhamsted,
Herts.
*November 20th*, 1961.

### Neonatal Scouring in Piglets

Sir,—The correspondents in your issue of November 18th, 1961, have rightly indicated the complicating factor of antibiotic resistance to *E. coli* in the treatment of this disease.

We have frequently found strains of *E. coli* associated with outbreaks to be resistant to one or more of the commonly used therapeutic agents, *i.e.* streptomycin, chloramphenicol, the tetracyclines and the sulphonamides; a few strains have been resistant to all these agents. However, we have never found a strain resistant to neomycin and consequently, we use and recommend this antibiotic. The usual dosage, *per os*, is 30 mg. neomycin sulphate in approximately 0.5 ml. of water, twice daily. Since the volume of vehicle used is small it can be squirted easily into the mouth by means of a syringe or small pipette without any distress to the piglet.

Yours faithfully,
H. WILLIAMS SMITH.
J. E. T. JONES.

The Animal Health Trust,
Farm Livestock Research Centre,
Stock,
Essex.
*November 20th*, 1961.

### Louping-ill in the West of Scotland

Sir,—In comment of our statement that "Central Scotland was apparently unaffected by louping-ill, as no evidence of louping-ill antibodies were found in sera collected from 204 sheep and 314 cattle in Stirlingshire, from August to November, 1960," your abstract in THE VETERINARY RECORD of October 21st observes that we did not state if these were healthy or sick animals. We regret this omission. Both sheep and cattle were healthy. Mr. Grant, Deputy Regional Veterinary Officer, who organised the collection of the sera, has since informed us that although the animals were slaughtered in Stirling they came from adjoining counties in Central Scotland and included Perth, Stirling, Clackmannan, Dumbarton, Argyll, Fife, and Kinross.

Yours faithfully,
CONSTANCE A. C. ROSS.
CATHERINE H. GOURLAY.

University Department of Virology,
Ruchill Hospital,
Glasgow.
*November 16th*, 1961.

**DISEASES OF ANIMALS ACT, 1950—GREAT BRITAIN**
**Summary of Returns of Confirmed Outbreaks of Scheduled (Notifiable) Diseases**

| Period | | Anthrax | Atrophic Rhinitis | Foot-and-Mouth | Fowl Pest | Sheep Scab | Swine Fever |
|---|---|---|---|---|---|---|---|
| 16th to 31st October, 1961 | | 11 | — | — | 41 | — | 37 |
| Corresponding period in | 1960 | 8 | — | 2 | 94 | — | 73 |
| | 1959 | 12 | — | — | 118 | — | 75 |
| | 1958 | 5 | — | 1 | 33 | — | 43 |
| 1st January to 31st October, 1961 | | 191 | — | 103 | 953 | — | 922 |
| Corresponding period in | 1960 | 169 | 1 | 30 | 1,590 | — | 1,002 |
| | 1959 | 208 | 2 | 9 | 728 | — | 1,058 |
| | 1958 | 137 | 5 | 116 | 617 | — | 1,069 |